Available online at www.derpharmachemica.com

ISSN 0975-413X
CODEN (USA): PCHHAX

Der Pharma Chemica, 2017, 9(13):55-60
(http://www.derpharmachemica.com/archive.html)

Structural Elucidation, Characterization, Crystal Structure and Hirshfeld Surface Analysis of 1-(2,4,5-trimethoxy-phenyl)-2-nitropropene

Suvarna Shenvi[1], Chandrasekara Reddy G[1], Naveen S[2], Lokanath NK[3], Ananda Kumar CS[4,5*]

[1]*Chemical Science Division, Vittal Mallya Scientific Research Foundation, J.C. Industrial layout, Kanakapura road, Bangalore, Karnataka-560062, India*
[2]*Institution of Excellence, Vijnana Bhavana, Manasagangotri, University of Mysore, Mysuru-570 006, India*
[3]*Department of Studies in Physics, Manasagangotri, University of Mysore, Mysuru-570 006, India*
[4]*Department of Nanotechnology, Visvesvaraya Technological University CPGS, Muddenahalli, Bengaluru region-562101, India*
[5]*Centre for Materials Science, Vijnana Bhavan, University of Mysore, Manasagangotri, Mysore-570 006, India*

ABSTRACT

The title compound was prepared from β-asarone (2, 4, 5-trimethoxy-(Z)-1-propenylbenzene) (1) on nitration with $AgNO_2/I_2$ and characterized using Infra-red (IR), Proton Nuclear Magnetic Resonance (^{1}H-NMR), 1D NOESY, Carbon-13 Nuclear Magnetic Resonance (^{13}C-NMR), Gas Chromatography/Mass Spectrometry (GC/MS) spectra and finally the structure was confirmed by X-ray Diffraction (XRD) studies. The compound crystallizes in the monoclinic space group $P2_1$ with the C=C olefinic double bond in both the molecules adopting an E conformation. The structure exhibits both inter and intramolecular hydrogen bonds of the type C-H...O and contributes to the crystal packing. Further, the Hirshfeld surface analysis reveals the nature of intermolecular contacts; the fingerprint plot provides the information about the percentage contribution from the intermolecular contacts to the surface.

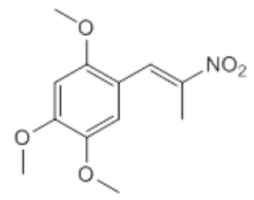
Keywords: β-asarone, 2-nitropropene, Crystal structure, Hirshfeld Surface, E-conformation, C-H…O Hydrogen bonds

INTRODUCTION

Asarone, which includes both alpha and beta types, is an ether found in *Acorus calamus* is generally used for treatment of cough, fever, bronchitis, inflammation, depression, tumours, haemorrhoids, skin diseases, insomnia, hysteria, epilepsy and loss of memory [1,2]. While β-asarone was the main constituent of rhizomes of *A. calamus* [3], α-asarone was isolated as a minor component from the rhizomes of related species *Acorus gramineus* [4]. Comparative study of genotoxicity and cytotoxicity of β-asarone and α-asarone was investigated and found that α-asarone was more toxic in the HepG2 cell system [5-7]. β-asarone may be a potential candidate for development as a therapeutic agent in alzheimer's disease [8]. In continuation of our research on β-asarones [9,10], herein, spectral characterization, crystal structure and Hirshfeld surface analysis of the title compound is reported. Further, Hirshfeld surface analysis including d_{norm} surfaces and 2D Fingerprint plots (FP) were performed and the results of the analysis are discussed.

MATERIALS AND METHODS

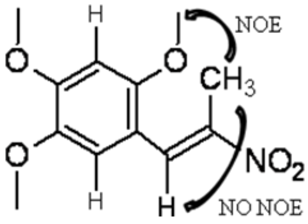
Commercially available chemicals were used directly as received. Instrumental details, the experimental procedure and analytical data for the compound have been reported [11]. A white coloured rectangle shaped single crystal of dimensions 0.29 × 0.26 × 0.22 mm of the title compound was chosen for an X-ray diffraction study. The X-ray intensity data were collected at a temperature of 296 K on a Bruker Proteum2 CCD diffractometer equipped with an X-ray generator operating at 45 kV and 10 mA, using CuK_α radiation of wavelength 1.54178 Å. Data were collected for 24 frames per set with different settings of φ (0° and 90°), keeping the scan width of 0.5°, exposure time of 2 s, the sample to detector distance of 45.10 mm and 2θ value at 46.6°. A complete data set was processed using SAINT PLUS [12].



Scheme 1: Compound 1

NOE experiment for the compound 1

When the methyl peak in Proton Nuclear Magnetic Resonance (^{1}H-NMR) at δ=2.42 was irradiated, no NOE enhancement of phenyl proton or the olefinic proton was observed indicating that compound 1 is 1-(2,4,5-trimethoxy phenyl)-(*E*)-2-nitropropene (Figure 1). In proton NMR, the methoxy group at 2-position shows enhancement and relatively shifts over the other two methoxy groups indicating that this methoxy group falls in the shielding cone of nitro group indicating its *E*-orientation (Schemes 1 and 2).



Scheme 2: *E*-orientation

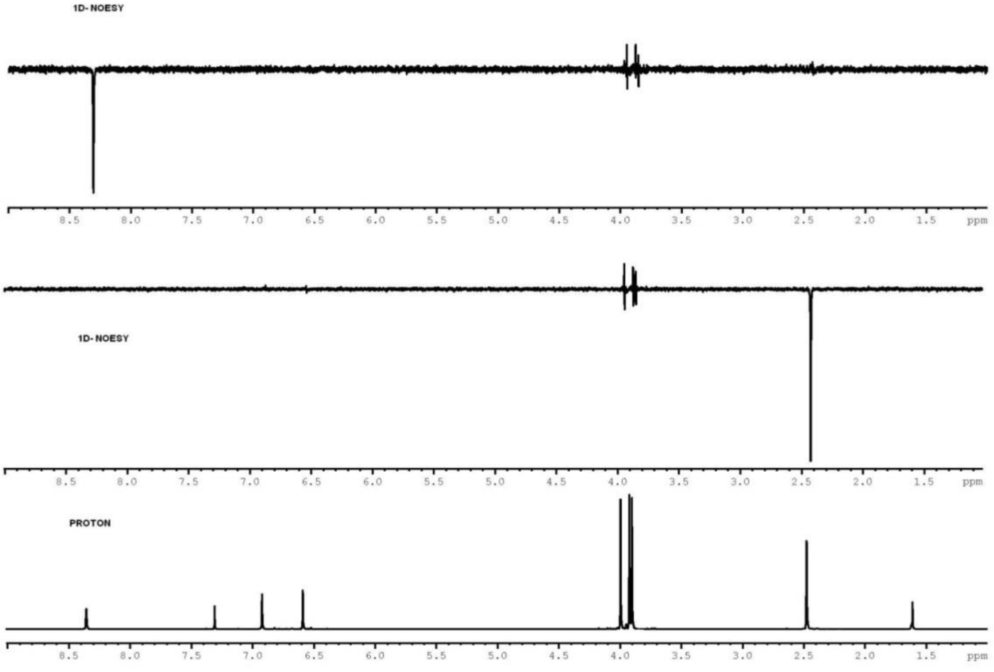


Figure 1: 1D NOESY experiment with proton NMR of 1-(2,4,5-trimethoxy-phenyl)-2-nitropropene

Crystal structure determination and Hirshfeld surface calculations

The crystal structure was solved by direct methods and refined by full-matrix least squares method on F^2 using SHELXS and SHELXL programs [13]. All the non-hydrogen atoms were revealed in the first difference fourier map itself. All the hydrogen atoms were positioned geometrically. After ten cycles of refinement, the final difference Fourier map showed peaks of no chemical significance and the residuals saturated to 0.0301. The geometrical calculations were carried out using the program PLATON [14]. The molecular and packing diagrams were generated using the software MERCURY [15]. The details of the crystal structure and data refinement are given in Table 1.

The list of bond lengths and bond angles of the non-hydrogen atoms are given in Tables 2 and 3 respectively. Figure 2 represents the ORTEP of the molecule with thermal ellipsoids drawn at 50% probability. 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, plotting 2D fingerprint plots [17,18] and generating electrostatic potential [19] with TONTO [20,21]. The electrostatic potential was 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. 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).

Table 1: Crystal data and structure refinement table

Parameter	Value
CCDC deposit No.	CCDC 1534444
Empirical formula	$C_{12}H_{15}O_5N$
Formula weight	253.25
Temperature	293(2) K
Wavelength	1.54178 Å
Crystal system, space group	Monoclinic, $P2_1$
Unit cell dimensions	a=9.9508(2)Å b=9.5623(2)Å c=12.7917(3)Å β=12.7917(3)°
Volume	1214.49(5) $Å^3$
Z, Calculated density	4, 1.385 Mg/m^3
Absorption coefficient	0.916 mm^{-1}
$F_{(000)}$	536
Crystal size	0.29 × 0.26 × 0.22 mm
Theta range for data collection	4.45° to 64.34°
Limiting indices	$-10 \leq h \leq 11$, $-10 \leq k \leq 10$, $-12 \leq l \leq 14$
Reflections collected/unique	3059/2636 [R(int)=0.0198]
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	2636/1/333
Goodness-of-fit on F^2	1.044
Final R indices [I>2σ(I)]	R1=0.0301, wR2=0.0824
R indices (all data)	R1=0.0303, wR2=0.0827
Largest diff. peak and hole	0.145 and −0.148 e. $Å^{-3}$

Table 2: Bond lengths (Å)

Atoms	Length	Atoms	Length
O5A-C8A	1.370(2)	C6B-C7B	1.386(3)
O5A-C12A	1.437(2)	C6B-C5B	1.398(3)
O5B-C8B	1.371(2)	C6A-C7A	1.388(3)
O5B-C12B	1.426(2)	C6A-C5A	1.397(3)
O3B-C5B	1.360(2)	C8A-C9A	1.382(3)
O3B-C10B	1.430(2)	C8A-C7A	1.408(3)
O4B-C7B	1.365(2)	C8B-C9B	1.378(3)
O4B-C11B	1.434(2)	C8B-C7B	1.409(3)
O2A-N1A	1.237(2)	C4A-C5A	1.398(3)
O4A-C7A	1.364(2)	C4A-C9A	1.399(3)
O4A-C11A	1.431(2)	C4A-C3A	1.468(3)
O2B-N1B	1.235(2)	C5B-C4B	1.402(3)
O3A-C5A	1.371(2)	C1A-C3A	1.339(3)
O3A-C10A	1.428(2)	C1A-C2A	1.489(3)
O1A-N1A	1.229(2)	C4B-C9B	1.403(3)
O1B-N1B	1.227(2)	C4B-C3B	1.453(2)
N1A-C1A	1.471(2)	C3B-C1B	1.338(2)
N1B-C1B	1.468(2)	C1B-C2B	1.490(3)

Table 3: Bond angles (°)

Atoms	Angle	Atoms	Angle
C8A-O5A-C12A	116.20(14)	O3B-C5B-C4B	116.06(15)
C8B-O5B-C12B	116.07(14)	C6B-C5B-C4B	120.76(17)
C5B-O3B-C10B	118.11(14)	C8A-C9A-C4A	121.49(16)
C7B-O4B-C11B	116.45(14)	C3A-C1A-N1A	115.59(18)
C7A-O4A-C11A	117.21(15)	C3A-C1A-C2A	129.46(18)
C5A-O3A-C10A	117.85(14)	N1A-C1A-C2A	114.68(16)
O1A-N1A-O2A	122.87(17)	O4A-C7A-C6A	124.14(15)
O1A-N1A-C1A	118.03(18)	O4A-C7A-C8A	115.09(16)
O2A-N1A-C1A	119.11(15)	C6A-C7A-C8A	120.76(16)
O1B-N1B-O2B	122.66(15)	C5B-C4B-C9B	118.28(15)
O1B-N1B-C1B	117.93(15)	C5B-C4B-C3B	118.63(16)
O2B-N1B-C1B	119.42(14)	C9B-C4B-C3B	122.92(17)
C7B-C6B-C5B	119.59(16)	C1A-C3A-C4A	126.26(18)
C7A-C6A-C5A	119.37(16)	C8B-C9B-C4B	121.70(16)
O5A-C8A-C9A	125.83(16)	O3A-C5A-C6A	123.28(15)
O5A-C8A-C7A	115.28(15)	O3A-C5A-C4A	115.94(15)
C9A-C8A-C7A	118.88(16)	C6A-C5A-C4A	120.79(17)
O5B-C8B-C9B	125.37(16)	C1B-C3B-C4B	128.17(16)
O5B-C8B-C7B	115.53(15)	C3B-C1B-N1B	115.80(15)
C9B-C8B-C7B	119.04(16)	C3B-C1B-C2B	130.01(16)
C5A-C4A-C9A	118.71(16)	N1B-C1B-C2B	114.05(15)
C5A-C4A-C3A	118.20(17)	O4B-C7B-C6B	123.32(15)
C9A-C4A-C3A	122.82(15)	O4B-C7B-C8B	116.18(16)
O3B-C5B-C6B	123.18(16)	C6B-C7B-C8B	120.49(15)

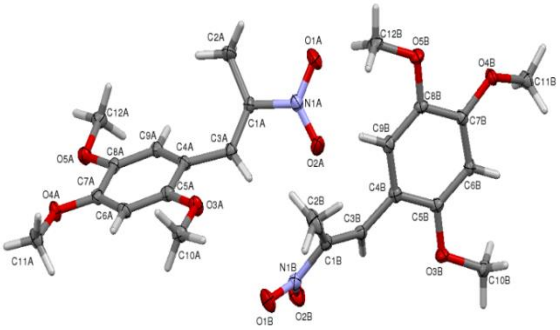


Figure 2: ORTEP of the molecule with thermal ellipsoids drawn at 50% probability

RESULTS AND DISCUSSIONS

There are two molecules in the asymmetric unit. The C=C olefinic double bond in both the molecules adopts an *E*-conformation. The trans configuration of the C3A=C1A/C3B=C1B double bonds in both the molecules is confirmed by the torsion angle values of 179.83(16)° and 176.93(18)° for C4A-C3A-C1A-N1A and C4B-C3B-C1B-N1B respectively. The methoxy groups in both the molecules lie in the plane of the phenyl rings whereas the nitro propene moiety deviates by 179.83(16)° and 176.93(18)° respectively as indicated by the torsion angle values for C4A/C3A/C1A/N1A and C4B/C3B/C1B/N1B respectively. The structure exhibits both inter and intra-molecular hydrogen bonds of the type C-H...O. These hydrogen bonds links the molecules to form chains along the *c* axis (Figure 3) and the molecules appear to be stacked when viewed down along the *b* axis (Figure 4).

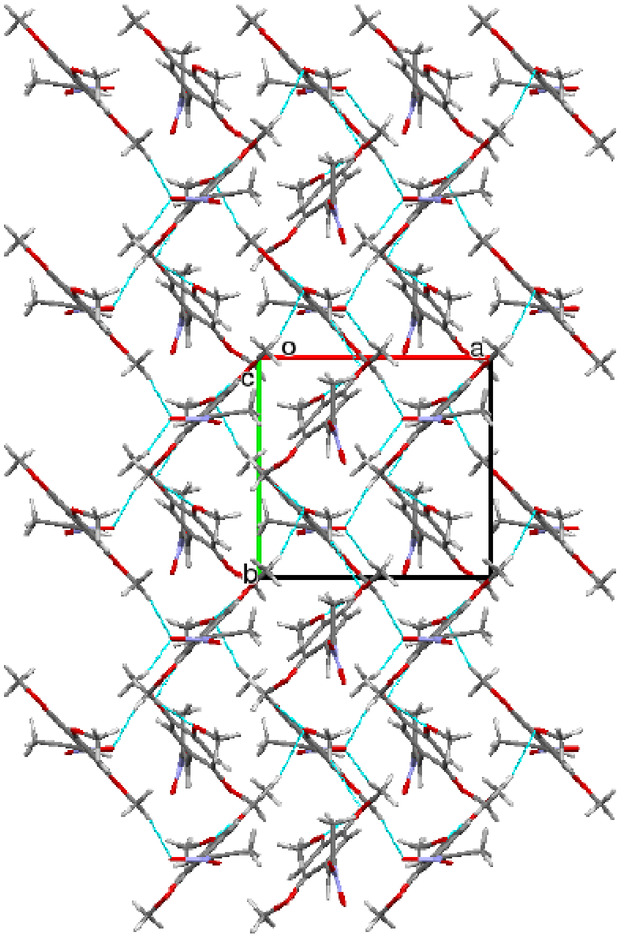


Figure 3: Packing of the molecules when viewed down along the *c* axis. The blue dotted lines represent intermolecular hydrogen bonds

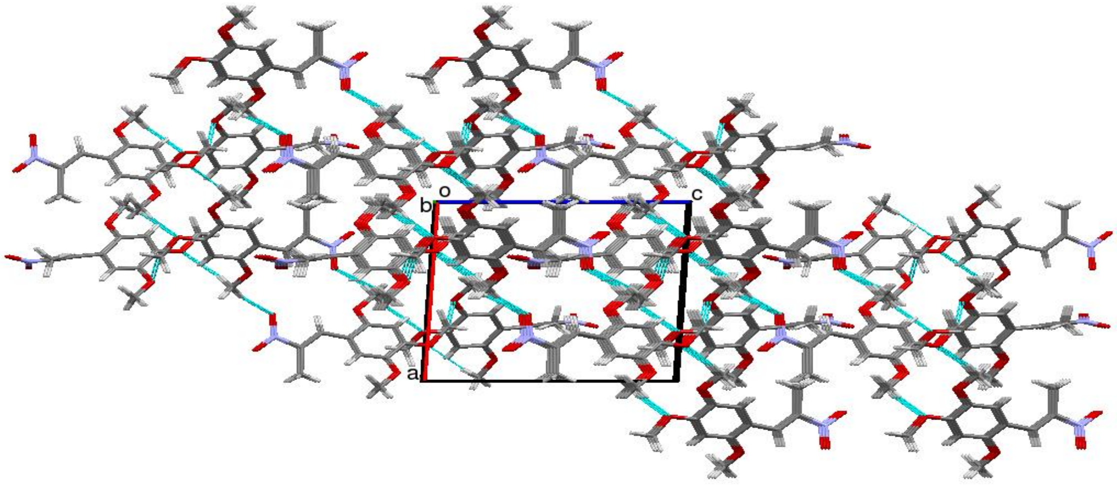


Figure 4: Packing of the molecules when viewed down along the b axis exhibiting layered stacking. The blue dotted lines represent intermolecular hydrogen bonds

Hirshfeld surface analysis is an effective tool for exploring packing modes and intermolecular interactions in molecular crystals, as they provide a visual picture of intermolecular interactions and of molecular shapes in a crystalline environment. Surface features characteristic of different types of intermolecular interactions can be identified, and these features can be revealed by colour coding distances from the surface to the nearest atom exterior (d_e plots) or interior (d_i plots) to the surface. This gives a visual picture of different types of interactions present and also reflects their relative contributions from molecule to molecule. Further, 2D fingerprint plots (FP), in particular the breakdown of FP into specific atom…atom contacts in a crystal, provide a quantitative idea of the types of intermolecular contacts experienced by molecules in the bulk and presents this information in a convenient color plot. Hirshfeld surfaces comprising d_{norm} surface and Finger Print plots were generated and analyzed for the title compound in order to explore the packing modes and intermolecular interactions. The two dimensional fingerprint plots from Hirshfeld surface analyses Figure 5, illustrates the difference between the intermolecular interaction patterns and the relative contributions to the Hirshfeld surface (in percentage) for the major intermolecular contacts associated with the title compound. The fingerprint plots can be decomposed to highlight particular atoms pair close contacts. Importantly, H...H (39.2%) bonding appears to be a major contributor in the crystal packing, whereas the C...H/H...C (19.5%), O...H/H...O (37.4%), plots also reveal the information regarding the intermolecular hydrogen bonds thus supporting for the intermolecular interactions. This intermolecular contact is highlighted by conventional mapping of d_{norm} on molecular Hirshfeld surfaces and is shown in Figure 6. The red spots over the surface indicate the intercontacts involved in hydrogen bond. The dark-red spots on the d_{norm} surface arise as a result of the short interatomic contacts, i.e., strong hydrogen bonds, while the other intermolecular interactions appear as light-red spots.

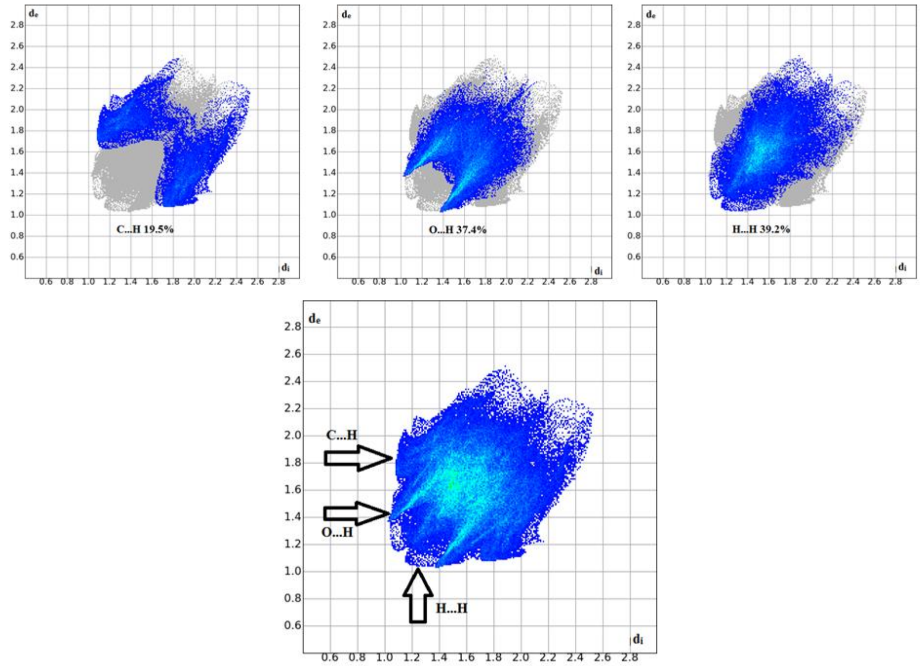


Figure 5: Fingerprint plots of the title compound showing H...H, C…H, O...H and N...H interactions. d_i is the closest internal distance from a given point on the Hirshfeld surface and d_e is the closest external contacts

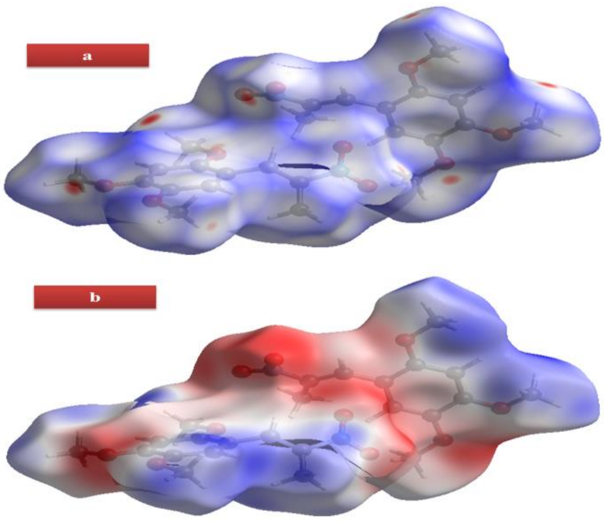


Figure 6: (a) d_{norm} and (b) electrostatic potential mapped on Hirshfeld surface for visualizing the intermolecular contacts

ACKNOWLEDGMENTS

The authors are thankful to the Institution of Excellence, Vijnana Bhavana, University of Mysore, Manasagangotri, Mysore, for providing the single-crystal X-ray diffraction data. The authors SS and GC are thankful to Vittal Mallya Scientific Research Foundation, Bangalore, for providing the research facility.

CONCLUSION

1-(2,4,5-Trimethoxy phenyl)-2-nitropropene was prepared from β-asarone (2,4,5-trimethoxy-(*Z*)-1-propenylbenzene) on nitration with $AgNO_2/I_2$ and was spectroscopically characterized using IR, ^{1}H-NMR, 1D NOESY, ^{13}C-NMR, GC-MS spectra and finally the structure was confirmed by X-ray diffraction studies. The compound crystallizes in the monoclinic crystal system with the space group $P2_1$ with the C=C olefinic double bond in both the molecules adopting an *E* conformation. The structure exhibited both inters and intramolecular hydrogen bonds of the type C--H...O which links the molecules to form chains. Further, H...H (39.2%) bonding appears to be a major contributor in the crystal packing, whereas the C...H/H...C (19.5%), O...H/H...O (37.4%), plots also reveal the information regarding the intermolecular hydrogen bonds thus supporting for the intermolecular interactions.

REFERENCES

[1] S.R. Yende, U.N. Harle, D.T. Rajgure, T.A. Tuse, N.S. Vyawahare, *Pharmacog. Rev*., **2008**, 2(4), 22-26.
[2] A.E. Raja, M. Vijayalakshmi, G. Devalarao, *Res. J. Pharm. Technol*., **2009**, 2, 256-261.
[3] A.K. Sinha, B.P. Joshi, R. Acharya, US Patent US6590127 B1, **2003**.
[4] J.Y. Lee, B.S. Yun, B.K. Hwang, *J. Agric. Food Chem*., **2004**, 52(4), 7760-780.
[5] D.J. Zou, G. Wang, J.C. Liu, *Pharmazie*., **2011**, 66(1), 44-51.
[6] P. Unger, M.F. Melzig, *Sci. Pharm*., **2012**, 80(3), 663-668.
[7] X. Zou, S.L. Liu, J.Y. Zhou, J. Wu, B.F. Ling, R.P. Wang, *Asian Pac. J. Cancer Prev*., **2012**, 13(10), 5291-5298.
[8] Y. Geng, C. Li, J. Liu, G. Xing, L. Zhou, M. Dong, X. Li, Y. Niu, *Biol. Pharm. Bull*., **2010**, 33(5), 836-843.
[9] S. Shenvi, K. Kumar, K.S. Hatti, K. Rijesh, L. Diwakar, G.C. Reddy, *Eur. J. Med. Chem.*, **2013**, 62, 435-442.
[10] S. Shenvi, Vinod, R. Hegde, A. Kush, G.C. Reddy, *J. Med. Plant Res*., **2011**, 5(20), 5132-5137.
[11] S. Shenvi, Latha Diwakar, G.C. Reddy, *Int. J. Med. Chem*., **2014**.
[12] Bruker, APEX. SAINT, Bruker, AXS Inc., Madison, Wisconsin, USA, **2004**.
[13] G.M. Sheldrick, *Acta Cryst*., **1990**, 46, 467-473.
[14] G.M. Sheldrick, *Acta Cryst*., **2015**, 71(1), 3-8.
[15] A.L. Spek, *Acta Cryst*., **1990**, 46(s1), c34-c34.
[16] C.F. Macrae, I.J. Bruno, J.A. Chisholm, P.R. Edgington, P. McCabe, E. Pidcock, L.M. Rodriguez, R. Taylor, J. van de Streek, P.A. Wood, *J. Appl. Cryst*., **2008**, 41, 466-470.
[17] S.K. Wolff, D.J. Grimwood, J.J. McKinnon, M.J. Turner, D. Jayatilaka, M.A. Spackman, Crystal Explorer (Version 3.0), University of Western Australia, **2012**.
[18] S.K. Seth, *Cryst. Engg. Comm*., **2013**, 15, 1772-1781.
[19] S.K. Seth, *J. Mol. Struct*., **2014**, 1064, 70-75.
[20] M.A. Spackman, J.J. McKinnon, D. Jayatilaka, *Cryst. Engg. Comm*., **2008**, 10(4), 377-388.
[21] D. Jayatilaka, D.J. Grimwood, A. Lee, A. Lemay, A.J. Russel, C. Taylo, S.K. Wolff, The University of Western Australia, Nedlands, Australia, **2005**.