SYNTHESIS, SPECTROSCOPIC CHARACTERIZATION, X-RAY ANALYSIS OF DMSO SOLVATED 5'-CHLORO-1H,1"H-[3,3':3',3"-TERINDOL]-2'(1'H)-ONE

Sakshi Sharma[a], Goutam Brahmachari[b], Bubun Banerjee[b], Rajni Kant[a] and Vivek K. Gupta[a]*

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The title compound 5'-chloro-1H,1"H-[3,3':3',3"-terindol]-2'(1'H)-one is synthesized via one-pot multicomponent reaction (MCR) at room temperature using commercially available sulfamic acid as inexpensive and environmentally benign organo-catalyst. It crystallizes in the monoclinic space group $P2_1/n$ with the unit-cell parameters: a = 15.3117(15), b = 10.9302(8), c = 16.591(2) Å, α = 90.00° β = 98.224(10)°, γ = 90.00° and Z = 4. The crystal structure was solved by direct methods using single-crystal X-ray diffraction data collected at room temperature and refined by full-matrix least-squares procedures to a final R-value of 0.0735 for 2539 observed reflections. Both the DMSO solvent molecules take part in the inter- and intramolecular interactions that are responsible for the formation of hydrogen bonded network. Two C-H···π inter-molecular hydrogen bonds are also present in the crystal structure.

*Corresponding Authors
Mob: +91 9419102467
E-Mail: vivek_gupta2k2@hotmail.com
[a] X-ray Crystallography Laboratory, Post-Graduate Department of Physics & Electronics, University of Jammu, Jammu Tawi - 180 006, India
[b] Laboratory of Natural Products & Organic Synthesis, Department of Chemistry, Visva-Bharati (a Central University), Santiniketan – 731235, West Bengal, India.

Introduction

Bis(indolyl)indolin-2-ones represent a "privileged" structural motif well distributed in naturally occurring compounds[1] possessing a broad spectrum of biological activities, such as anti-inflammatory,[2] anti-HIV,[3] antitumor[4] activities etc. Investigation of the structural features of biologically relevant bis(indol-3-yl)indolinone derivatives is, thus, of considerable interest to the researchers. In this communication, we wish to report on the green synthesis of one such derivative, namely 5'-chloro-1H,1"H-[3,3':3',3"-terindol]-2'(1'H)-one via one-pot multicomponent reaction at room temperature using commercially available sulfamic acid as inexpensive and environmentally benign organo-catalyst, and its crystal structure. The structure of the title compound was elucidated by detailed spectral methods and XRD studies.

Experimental

Synthesis

The synthesis of the title compound, 5'-chloro-1*H*,1"*H*-[3,3':3',3"-terindol]-2'(1'*H*)-one (**1**), was carried out via one-pot multi-component reaction in aqueous ethanol using low-cost and environmentally benign sulfamic acid as catalyst at room temperature. An oven-dried screw cap test tube was charged with a magnetic stir bar, indole (0.117 g, 1 mmol), 5-chloroisatin (0.090 g, 0.5 mmol), sulfamic acid (0.009 g, 20 mol % as organo-catalyst), and EtOH-H_2O (1:1 v/v; 4 ml) in a sequential manner; the reaction mixture was then stirred vigorously at room temperature for 3 h.[5] The progress of the reaction was monitored by TLC. On completion of the reaction, a solid mass precipitated out that was filtered-off followed by washing with aqueous ethanol. The white solid mass was then subjected to recrystallization from aqueous ethanol to obtain pure title compound (0.170 g, yield 86 %) with the m.p. 567-569 K. The structure of (**1**) was confirmed by analytical as well as spectral studies including FT-IR, ^{1}H NMR, ^{13}C NMR, and TOF-MS. Unit crystal was obtained from DMSO as a solvent. For crystallization, 50 mg of the compound dissolved in 5 ml DMSO and left for several days at ambient temperature which yielded white block shaped crystals. The chemical structure of the title compound is given in Figure 1.

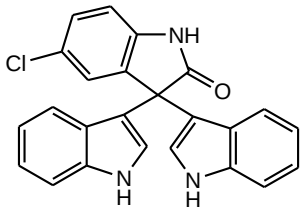

Figure 1. Chemical structure of the title compound.

5'-Chloro-1*H*,1''*H*-[3,3':3',3''-terindol]-2'(1'*H*)-one

This compound was obtained as white solid (0.170 g, 86 %). m.p. 567-569 K. IR (KBr): 3356, 3119, 3053, 2969, 1701, 1614, 1534, 1474, 1425, 1335, 1236, 1171, 1113, 1005, 876, 824, 750 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) δ = 11.04 (1H, s, -N*H*), 11.03 (s, 1H, -N*H*), 10.78 (s, 1H, -N*H*), 7.38 (2H, d, J = 8.4 Hz, aromatic H), 7.30 (1H, dd, J = 8.0, 2.4 & 2.0 Hz, aromatic H), 7.23 (1H, br s, aromatic H), 7.21-7.17 (2H, m, aromatic H), 7.05 (2H, d, J = 7.2 Hz, aromatic H), 7.02 (1H, t, J = 4.4 & 4.0 Hz, aromatic H),

6.90 (2H, d, *J* = 2.4 Hz, aromatic H), 6.83 (2H, t, *J* = 7.6 & 7.2 Hz, aromatic H). ^{13}C NMR (100 MHz, DMSO-d_6) δ = 178.80, 140.69, 137.35 (2C), 137.02, 128.27, 125.91 (2C), 125.85 (2C), 125.09, 124.84 (2C), 121.49 (2C), 120.93 (2C), 118.84 (2C), 113.91, 112.16 (2C), 111.54, 53.26. TOF-MS 420.0881 [M + Na]$^+$. Anal. Calcd. for $C_{24}H_{16}ClN_3O$: C, 72.45, H, 4.05, N, 10.56. **F**ound: C, 72.47, H, 4.03, N, 10.54.

X-Ray Structure determination

X-ray intensity data of 9775 reflections (of which 4821 were unique) were collected on *X'calibur* CCD area-detector diffractometer equipped with graphite monochromated MoK_α radiation (λ = 0.71073 Å). The crystal used for data collection was of dimensions 0.30 x 0.20 x 0.20 mm. The cell dimensions were determined by least-squares fit of angular settings of 1851 reflections in the θ range 3.61º to 24.31º**.** The intensities were measured by ω scan mode for θ ranges 3.52º to 25.00º. 2539 reflections were treated as observed ($I > 2\sigma(I)$). Data were corrected for Lorentz, polarization and absorption factors. The structure was solved by direct methods using SHELXS97.[5] All non-hydrogen atoms of the molecule were located in the best E-map. Full-matrix least-squares refinement was carried out using SHELXL97.[6] The final refinement cycles converged to an $R = 0.0735$ and w$R(F^2) = 0.1818$ for the observed data. Residual electron densities ranged from $-0.431 < \Delta\rho < 0.385$ eÅ^{-3}. Atomic scattering factors were taken from International Tables for X-ray Crystallography (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4). The crystallographic data are summarized in Table 1.

Table 1. Crystal data and other experimental details.

CCDC Number	**1413889**
Crystal description	Block
Crystal size	0.30 x 0.20 x 0.20 mm
Empirical formula	$C_{28}H_{28}ClN_3O_3S_2$
Formula weight	554.10
Radiation, Wavelength	Mo *K*α, 0.71073 Å
Unit cell dimensions	*a*= 15.3117(15) Å
	b = 10.9302(8) Å
	c= 16.591(2) Å
	α= 90.00º
	β = 98.224(10) º
	γ= 90.00º
Crystal system, space group	monoclinic , P 21/n
Unit cell volume	742.79(9)Å^3
No. of molecules per unit cell, Z	4
Absorption coefficient	0.326 mm^{-1}
F(000)	1160
θ range for entire data collection	3.52 <θ< 25.00
Reflections collected / unique	9775/ 4821
Reflections observed $I > 2\sigma(I)$)	2539
Range of indices	*h*= -18 to 9
	k=--9 to 12
	l= -19 to 19
No. of parameters refined	354
Final *R*-factor	0.0735
w$R(F2)$	0.1818
R_{int}	0.0443
R_σ	0.0901
Goodness-of-fit	1.031
Final residual electron density	-0.431<Δρ<0.385 eÅ^{-3}

Result and Discussions

An ORTEP[7] view of the compound with atomic labeling is shown in Figure 2. The geometry of the molecule was calculated using the WinGX[8], PARST[9] and PLATON[10] software.

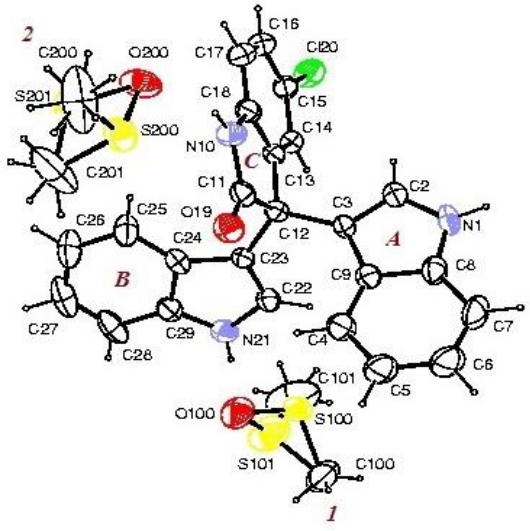

Figure 2. ORTEP view of the molecule with displacement ellipsoids drawn at 40 %. H atoms are shown as small spheres of arbitrary radii.

The asymmetric unit cell consists of the molecule of title compound. The best packing view has been obtained down b-axis (Figure 3). The asymmetric unit of title compound, '$C_{28}H_{28}ClN_3O_3S_2$, 2(C_2H_6OS)', comprises of two indole rings (*A*) and (*B*), an oxindole ring (*C*), connected through a carbon atom C12 and two DMSO solvent molecules (*1*) and (*2*). The oxindole ring is substituted by a chlorine atom at position C15.

In the molecule, the expected geometric parameters are observed. The geometry of both the indole rings, (*A*) and (*B*), indicates a high degree of similarity in terms of their bond lengths and bond angles and are in good agreement with the standard values.[11] The bond lengths and bond angles of the title molecule are quite close to the corresponding values in a related structure 3,3-bis(1H-indol-3-yl)indolin-2-one, ($C_{24}H_{17}N_3O$).[12]

The indole moieties are individually planar where as the five-membered ring in an oxindole system (N10/C11/C12/C13/C18) in the title compound deviates slightly from planarity and adopts a conformation halfway between that of half-chair and envelope with asymmetry parameters [$\Delta C2$(C11-C12) = 1.756] and [ΔC_s(C11) = 0.930].[13]

The dihedral angle between the planes defined by the constituent pyrrolidine and benzene rings in a chloro substituted oxindole ring is 1.42(14)°. By comparison, this angle is 4.22 (13)° in indole-3-carbaldehyde[14] and 0.29(11)° in indole-3-carboxylic acid[15]. The indole ring systems A and B make dihedral angle of 67.97(11)º with each other; the oxindole ring C is twisted with respect to these indole rings at angles 71.58(9)º and 82.38(9)º, respectively (Table 2).

Table 2. Selected bond lengths (Å), bond angles (º) and torsion angles(º) for non hydrogen atoms (e.s.d.'s are given in parentheses).

Bond distances(Å)		Bond angles(°)		Torsion angles(°)	
N1-C2	1.357(5)	N1-C8-C7	130.2(5)	C3-C12-C13-C14	69.9(5)
N1-C8	1.365(6)	C3-C9-C4	135.5(4)	O19-C11-C12-C13	-69.5(5)
N10-C11	1.356(5)	C3-C12-C13	110.3(3)	C11-C12-C23-C22	-143.5(4)
N10-C18	1.404(5)	N10-C18-C17	127.9(4)	C18-N10-C11-O19	174.9(4)
C11-O19	1.213(5)	C12-C13-C14	130.3(4)	C17-C16-C15-Cl20	-178.2(4)
C15-Cl20	1.741(5)	C11-C12-C23	111.5(3)	C23-C12-C13-C14	-57.2(5)
N21-C29	1.363(6)	C23-C24-C25	136.4(4)		
N21-C22	1.373(5)	N21-C29-C28	130.1(5)		

Table 3. Geometry of intermolecular hydrogen bonds.

D-H…A	D-H (Å)	H…A (Å)	D…A (Å)	θ[D-H…A (º)]
N1-H1..O200i	0.86	2.11	2.848(6)	143
N10-H10-O200ii	0.86	2.03	2.826(5)	154
N21-H21..S100ii	0.86	2.80	3.572(6)	150
N21-H21..O100ii	0.86	1.97	2.821(7)	170
C201-H20C...O19iii	0.96	2.46	3.378(9)	161
C200-H20G-Cl20i	0.96	2.82	3.574(9)	136
C17-H17...Cg1iv	0.93	2.74	3.662(5)	169
C25-H25...Cg2i	0.93	2.83	3.328(6)	114

Symmetry codes: (i) -x+1/2+1, -y-1/2, -z+1/2; (ii) x, y, z; (iii) -x+2, -y, -z; (iv) - x+3/2, y+1/2, -z+1/2

The C-Cl distance [C15-Cl20 = 1.741(5) Å] in an oxindole ring is comparable with the molecules of its type.[16,17] The N10—C18 and N10—C11 bond lengths [1.404(5) Å and 1.356(5) Å, respectively] differ from the corresponding mean values of 1.419 and 1.331 Å reported for γ –lactams[11]. The C11-O19 bond length [1.213(5) Å] is comparable with the mean value of 1.232 Å reported for γ – lactams.[18] The bond lengths N10-C11 and C11=O19 in the oxindole ring indicates hetero π- electron delocalization over atoms N10, C11 and O19. In particular, the contribution of the lone pair of electrons on the N atom to the N—C bond in the N**—**C=O group is revealed.

The average value of endocyclic angles in all three phenyl rings are close to 120º as expected for fully delocalized systems. The angles around atom C12 [C3–C12–C11=108.2(3)°, C3–C12–C13=110.3(3)°, C3–C12–C23=113.5(3)°, C11–C12–C13=101.0(3)°, C11–C12–C23=111.5(3)° and C13–C12–C23=111.6(3)°] deviate significantly from the ideal tetrahedral value of 109.4°. In the benzene rings of the the ring systems A, B and C, the endocyclic angles at C4-C9-C8=117.9(4)°, C25-C24-C29=118.7(4)°, C14-C13-C18=120.8(4)° are narrowed while those at C7-C8-C9=122.1(5)°, C24-C29-C28=121.6(5) and C13-C18-C17=122.0(4)° are widened from 120.0° respectively. This would appear to be a real effect caused by the fusion of the smaller pyrrole ring to the six-membered benzene ring, a feature commonly observed in indole derivatives. In both the solvent molecules 1 and 2, the S atoms are disordered over two sites with occupancy ratio of 0.636 : 0.363.

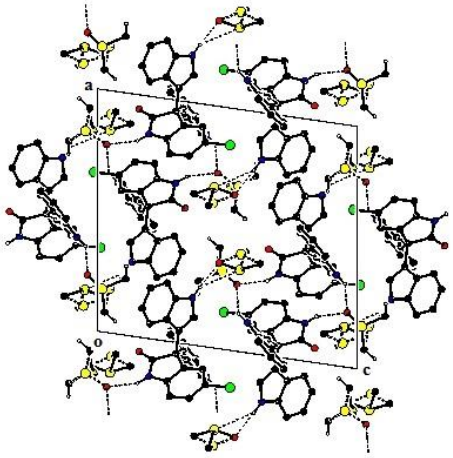

Figure 3. The packing arrangement of the molecules viewed down the b-axis.

The inter- and intramolecular hydrogen bonds are responsible for the formation of hydrogen bonded network thus, providing stability to the molecules in the unit cell. Both the DMSO solvents take part in the inter- and intramolecular interactions. In addition, two C–H···π inter-molecular hydrogen bonds are also observed in the crystal structure. The geometry of intra- and inter-molecular hydrogen bonds as well as C–H···π inter-molecular hydrogen bonds is given in (Table 3).

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References

[1]Kobayashi, M., Aoki, S., Gato, K., Matsunami, K., Kurosu, M., Kitagawa, I., *Chem. Pharm. Bull.*, **1994**, *42*, 2449-2451.

[2]Natarajan, A., Fan, Y. H., Chen, H., Guo, Y., Iyasere, J., Harbinski, F., Christ, W. J., Aktas, H., Halperin, J. A., *J. Med. Chem.*, **2004**, *47*, 1882.

[3]Bal, R. T., Anand, B., Yogeeswari, P., Sriram, D., *Bioorg. Med. Chem. Lett.*, **2005**, *15*, 4451.

[4]Tripathy, R., Reiboldt, A., Messina, P. A., Iqbal, M., Singh, J., Bacon, E. R., Angeles, Th. S., Yang, Sh. X., Albom, M. S., Robinson, C., *Bioorg. Med. Chem. Lett.*, **2006**, *16*, 2158.

[5]Brahmachari, G., Banerjee, B., *ACS Sustainable Chem. Eng.*, **2014**, 2, 2802.

[6]Sheldrick, G.M., *Acta Cryst.*, **2008**, *A64*, 112.

[7]Farrugia, L.J. *J Appl Cryst.*, **1997**, *30*, 565.

[8]Farrugia, L.J., *J Appl Cryst.*,**1999**, *32*, 837.

[9]Nardelli, M., *J Appl Cryst*., **1995**, *28*, 659.

[10]Spek, A.L., *Acta Cryst*., **2009**, *D65*, 148.

[11]Allen, F. H., Kennard,O., Watson,D.G., Brammer, L., Orpen,A.G., Taylor, R. *J. Chem.Soc., Perkin Trans-II.*, **1987**, S1.

[12]Selvanayagam, S., Mahesh Chandak, S., Velmurugan, D., Ravikumarc, K., Raghunathand, R., *Acta Cryst*., **2005**, *E61*, o3122.

[13]Duax, W. L., Norton, D. A., *Atlas of Steroid Structures, Plenum*, New York, **1975**, Vol. 1.

[14]Ng, S. W., *Acta Cryst*., **2007,** *E63*, o2732.

[15]Smith, G., Wermuth, U. D., Healy, P. C., *Acta Cryst.*, **2003,** *E59*, o1766.

[16]Hachula, B., Zerzucha, P., Zubko, M., Kusz, J., *Acta Cryst*., **2011**, *C67*, o413.

[17]Xing, X.-N., Li, L., Zhu, X.-Y., Chen, J.-R., *Acta Cryst*. **2007**, *E63*, o2969.

[18]Nerskov-Lauritsen, L., Burgi, H.-B., Hofmann, P., Schmidt, H. R., *Helv. Chim. Acta.*, **1985**, *68*, 76.

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