



STRUCTURE OF 5'-CHLORO-5,5''-DIFLUORO-1*H*,1''*H*- [3,3':3',3''-TERINDOL]-2'(1'*H*)-ONE

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The title compound 5'-chloro-5,5''-difluoro-1*H*,1''*H*-[3,3':3',3''-terindol]-2'(1'*H*)-one 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 $P2_1$ with the unit-cell parameters: $a = 10.193(5)$, $b = 9.012(5)$, $c = 13.406(5)$ Å, $\beta = 102.767(5)^\circ$ and $Z = 2$. 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 0.0390 for 1972 observed reflections. The molecules within the unit cell are stabilized by N-H...O and C-H...F type of hydrogen bonding. The sulphur atom of DMSO solvent molecule is found disordered over two set of sites S100 and S200 with occupancy ratio 0.70:0.30.

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Introduction

Bis(indolyl)indolin-2-ones are found to possess significant anti-inflammatory¹, anti-HIV², and antitumor³ activities. Hence, investigation of the structural features of biologically relevant bis(indol-3-yl)indolinone derivatives is of both scientific and practical interest. In this communication, we wish to report a one-pot synthesis of the 3,3-bis(indol-3-yl)indolinone derivative, namely 5'-chloro-5,5''-difluoro-1*H*,1''*H*-[3,3':3',3''-terindol]-2'(1'*H*)-one *via* multicomponent reaction (MCR) 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 spectral methods and XRD studies.

Experimental

Synthesis

The synthesis of the title compound, 5'-chloro-5,5''-difluoro-1*H*,1''*H*-[3,3':3',3''-terindol]-2'(1'*H*)-one, 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, 5-fluoroindole (0.135 g, 1 mmol), 5-chloroisatin (0.090 g, 0.5 mmol), sulfamic acid (0.009 g, 20 mol % as organo-catalyst),

and EtOH-H₂O (1:1 v/v; 4 ml) in a sequential manner; the reaction mixture was then stirred vigorously at room temperature for 4 h.⁴ 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 (0.166 g, yield 92 %) with the m.p. >573 K. The structure of 5'-chloro-5,5''-difluoro-1*H*,1''*H*-[3,3':3',3''-terindol]-2'(1'*H*)-one was confirmed by analytical as well as spectral studies including FT-IR, ¹H NMR, ¹³C 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.

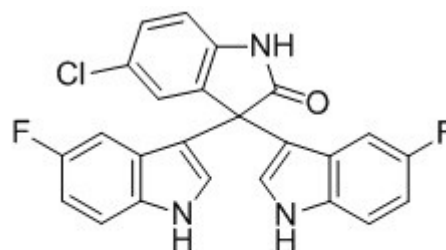


Figure 1. Chemical structure of title compound.

White solid. Yield: 92 %. M.p. >573 K. IR (KBr) ν_{\max} , cm⁻¹: 3414, 3350, 3119, 1699, 1624, 1578, 1533, 1474, 1296, 1236, 1177, 1113, 1068, 937, 806, 752. ¹H NMR (400 MHz, DMSO-*d*₆) δ /ppm: 11.20 (2H, s, -NH), 10.86 (s, 1H, -NH), 7.40 (2H, dd, $J = 8.8$ & 3.0 Hz, Ar-H), 7.33 (1H, dd, $J = 8.0$ and 2.0 Hz, Ar-H), 7.20 (1H, d, $J = 2.0$ Hz, Ar-H),

7.05 (1H, d, $J = 8.4$ Hz, Ar-*H*), 7.01 (2H, d, $J = 2.4$ Hz, Ar-*H*), 6.91 (2H, td, $J = 8.8, 2.8$ & 2.4 Hz, Ar-*H*), 6.86 (2H, dd, $J = 10.4, 2.8$ and 2.4 Hz, Ar-*H*). ^{13}C NMR (100 MHz, DMSO- d_6) δ /ppm: 178.59, 157.83, 155.53, 140.61, 136.22, 134.06 (2C), 128.58, 126.86 (2C), 126.13, 126.01, 125.91, 125.12, 113.82, 113.78, 113.32, 113.22, 111.77, 110.02, 109.76, 105.42, 105.19, 52.87. TOF-MS: 456.0689 [$\text{M} + \text{Na}$] $^+$. Elemental analysis: Calcd. (%) for $\text{C}_{24}\text{H}_{14}\text{ClF}_2\text{N}_3\text{O}$: C, 66.44; H, 3.25; N, 9.69; found: C, 66.41; H, 3.26; N, 9.71.

X-Ray Structure determination

X-ray intensity data of 5344 reflections (of which 2518 unique) were collected on *X'calibur* CCD area-detector diffractometer equipped with graphite monochromated $\text{MoK}\alpha$ radiation ($\lambda = 0.71073$ 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 1739 reflections in the θ range 4.02° to 26.40°. The intensities were measured by ω scan mode for θ ranges 3.63° to 26.00°. 1972 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 SHELXL97.⁵ The final refinement cycles converged to an $R = 0.0390$ and $wR(F^2) = 0.0727$ for the observed data. Residual electron densities ranged from $-0.193 < \Delta\rho < 0.158$ 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.

Result and discussions

An ORTEP⁶ view of the compound with atomic labeling is shown in Figure 2. The geometry of the molecule was calculated using the WinGX⁷, PARST⁸ and PLATON⁹ software.

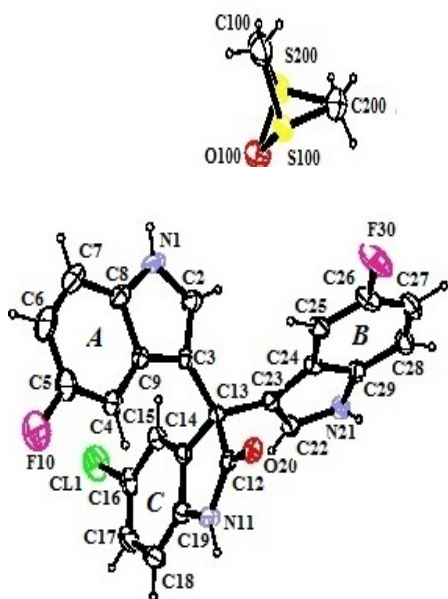


Figure 2. ORTEP view of the molecule of title compound

Table 1. Crystal data and other experimental details

CCDC Number	1056269
Crystal description	Block
Crystal size	0.30 x 0.20 x 0.20 mm
Empirical formula	$\text{C}_{26}\text{H}_{20}\text{ClF}_2\text{N}_3\text{O}_2\text{S}$
Formula weight	511.96
Radiation, Wavelength	$\text{Mo K}\alpha$, 0.71073 Å
Unit cell dimensions	$a = 10.193(5)$ Å $b = 9.012(5)$ Å $c = 13.406(5)$ Å $\alpha = 90.0^\circ$ $\beta = 102.767(5)^\circ$ $\gamma = 90.0^\circ$
Crystal system, space group	monoclinic, P2_1
Unit cell volume	$1201.0(10)$ Å 3
No. of molecules per unit cell, Z	2
Absorption coefficient	0.291 mm $^{-1}$
$F(000)$	528
θ range for entire data collection	$3.63 < \theta < 26.00$
Reflections collected / unique	5344 / 2518
Reflections observed $I > 2\sigma(I)$	1972
Range of indices	$h = -12$ to 12 $k = -10$ to 11 $l = -16$ to 15
No. of parameters refined	338
Final R -factor	0.0390
$wR(F^2)$	0.0727
R_{int}	0.0293
R_{sigma}	0.0477
Goodness-of-fit	0.985
Final residual electron density	$-0.193 < \Delta\rho < 0.158$ eÅ $^{-3}$

The asymmetric unit cell consists of the molecule of title compound and one DMSO solvent molecule. The sulphur atom of DMSO solvent molecule is found disordered over two set of sites S100 and S200 with occupancy ratio 0.70:0.30. Packing view of the molecules in the unit cell viewed down the a -axis is shown in Figure 3.

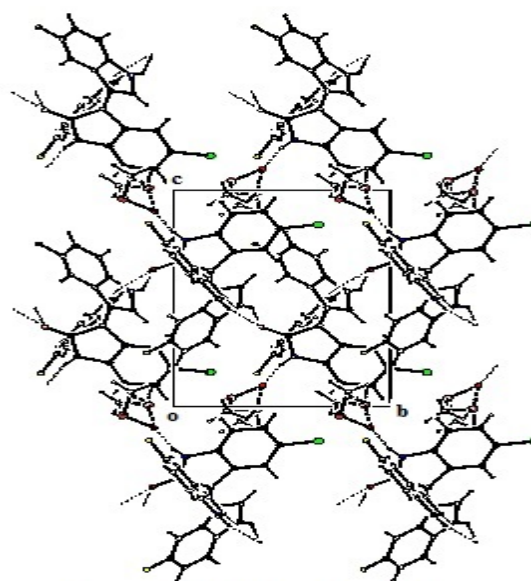


Figure 3. Packing view of the molecules down to a -axis.

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

Bond distances(Å)		Bond angles(°)		Torsion angles(°)	
N1-C2	1.362(4)	C2-N1-C8	109.3(3)	N11-C12-C13-C23	-109.3(3)
N1-C8	1.370(4)	C22-N21-C29	109.4(3)	N11-C12-C13-C3	126.4(2)
N21-C22	1.366(4)	C12-C13-C23	104.6(2)	C9-C4-C5-F10	177.9(3)
N21-C29	1.366(4)	C12-C13-C3	112.9(3)	C28-C27-C26-F30	-179.5(3)
C3-C13	1.513(4)	C2-C3-C9	106.7(2)		
C13-C23	1.518(4)	C22-C23-C24	106.8(2)		
Cl6-Cl1	1.736(4)	C13-C12-O20	126.2(3)		
C26-F30	1.363(4)	N11-C12-O20	125.1(3)		

Table 3. Geometry of intermolecular hydrogen bonds

D-H...A	D-H (Å)	H...A (Å)	D...A (Å)	∠[D-H...A (°)]
N1-H1...O20 ⁱ	0.87	2.131	2.289	167.58
N11-H11...O100 ⁱⁱ	0.86	1.884	2.728	166.24
N21-H21...O20 ⁱⁱⁱ	0.83	2.136	2.872	147.29
C200-H20C...F30 ^{iv}	0.96	2.453	3.053	120.38

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

The title compound comprises of three ring systems in which two are indole ring systems (A and B) and third is indolin-2-one ring system (C). All these ring systems are arbitrarily oriented with respect to each other and their mutual orientations are given by dihedral angles between them which are 64.40(6)^o between ring systems A and B, 86.97(7)^o between ring systems A and C and 80.59(6)^o between ring systems B and C respectively. All these ring systems are almost planar by themselves with maximum deviation from planarity observed for the atoms C6 by -0.0174 Å in ring system-A, C24 by -0.0057 Å in ring system B and C12 by -0.0814 Å in ring system-C respectively. The F10 fluorine atom lies below the mean plane of ring system A by -0.0530 Å whereas F30 fluorine atom lies exactly in the mean plane of ring system B. Both the oxygen atom O20 of carbonyl group and chlorine atom CL1 attached to ring system C lie below the mean plane of ring system by -0.1977 Å and -0.1815 Å. The bond distances N1-C2, N1-C8, N21-C22 and N21-C29 are 1.362(4) Å, 1.370(4) Å, 1.366(4) Å and 1.366(4) Å respectively which satisfy well with the corresponding values in some indole derivative structures.^{10,11} The bond distances C5-F10 and C26-F30 are 1.367(4) Å and 1.363(4) Å respectively, which satisfy well with the literature value. The endocyclic angle about nitrogen atoms N1 and N21 atoms of pyrrole rings are 109.3(3)^o and 109.4(3)^o which are close to each other and also to the corresponding angle in indole derivatives. The average value of endocyclic angles in all three phenyl rings are close to 120^o as expected for fully delocalized systems. The other bond lengths and bond angles are within the expected values¹² and are comparable to related structures. Selected bond lengths and bond angles are listed in the Table 2. The values of torsion angles N11-C12-C13-C23 and N11-C12-C13-C3 are -109.3(3)^o and 126.4(2)^o, reflect the disorientation of three ring systems. All other values of torsion angles are reasonable and some important torsion angles are listed in the Table 2.

Analysis of the crystal packing of title compound shows the presence of intermolecular C-H...F and N-H...O hydrogen bonds in the structure [Table 3]. The oxygen atom O20 of carbonyl group form hydrogen interactions with H1 and H21 attached to N1 and N21 respectively. In addition H11 attached to N11 form intermolecular hydrogen interaction with the oxygen atom O100 of solvent molecule. The H20C attached to carbon atom C200 of solvent molecule form hydrogen interaction with fluorine atom F30. In addition to these the crystal packing is also stabilized by weak hydrogen interactions.

Acknowledgments

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