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Crystal structure analysis of (2'S,3'S,4'S)-3'-(4-Chloro-2H-chromen-3-yl)-4'-(1H-indole-3-carbonyl)-1'-methyl-2-oxospiro[indoline-3,2'-pyrrolidine]-4'-carbonitrile

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Abstract: The Spiro pyrrolidine compound crystallizes in monoclinic P21/c space group with four molecules in the asymmetric unit. Crystal data were collected using BRUKER SMART APEX II CCD X-ray diffractometer. The structure was solved by direct method and refined on F^2 by full-matrix least-squares procedure to the final R_1 of 0.045 using SHELXL programs.
Key Words: Pyrrolidine, Indoline and crystal structure.

Introduction

Spiro-pyrrolidine derivatives are unique tetracyclic 5-HT(2A) receptor antagonists[1]. These derivatives possess anticonvulsant and anti-influenza virus[2] activities. Highly functionalized pyrrolidines have gained much interest in the past few years as they constitute the main structural element of many natural and synthetic pharmacologically active Compounds[3]. Optically active pyrrolidines have also been used as intermediates, chiral ligands or auxiliaries in controlled asymmetric synthesis[4].

Experimental

X-ray Structure Determination

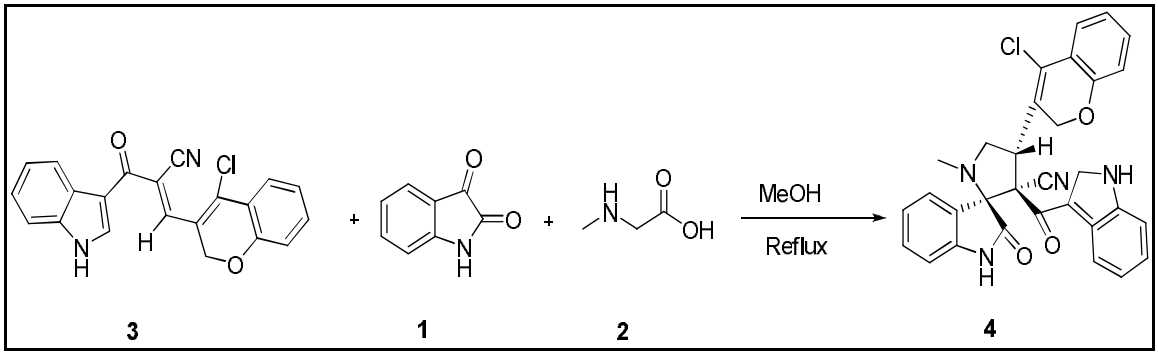
Single crystal of the compound suitable for x-ray diffraction was obtained by slow evaporation method. Three dimensional intensity data were collected on a Bruker[5] SMART APEX CCD Diffractometer using graphite monochromatized Mo-Kα radiation (λ= 0.71073 Å) at Department of chemistry, IIT, Chennai, India. The structure was solved by direct methods and refined on F^2 by full-matrix least-squares procedures using the SHELXL programs[6]. All the non-hydrogen atoms were refined using isotropic and later anisotropic thermal parameters. The hydrogen atoms were included in the structure factor calculation at idealized positions by using a riding model, but not refined. Images were created with ORTEP-3[7].The crystallographic data for the compound are listed in Table 1.

Table 1: Crystal data and structure refinement of the titled compound

Compound	**Parameters**
Empirical formula	$C_{31}H_{23}ClN_4O_3$
Formula weight	534.98
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P21/c
Unit cell dimensions	a = 20.4687(10) Å alpha = 90º b = 7.5619(2) Å beta = 105.7º c = 18.5834(8) Å gamma = 90º
Volume	2769.07(19) $Å^3$
Z, Calculated density	4, 1.283 Mg/m^3
Absorption coefficient	0.177 mm^{-1}
F(000)	1112
Crystal size	0.30 x 0.25 x 0.20 mm
Theta range for data collection	2.07 to 24.82 deg.
Limiting indices	-18<=h<=24, -8<=k<=7, -21<=l<=21
Reflections collected / unique	15918 / 4762 [R(int) = 0.0418]
Completeness to theta = 24.82	99.90%
Max. and min. transmission	0.9655 and 0.9488
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4762 / 2 / 362
Goodness-of-fit on F^2	0.996
Final R indices [I>2sigma(I)]	**R1 = 0.0450**, wR2 = 0.1038
R indices (all data)	R1 = 0.0773, wR2 = 0.1154
Extinction coefficient	0.0023(4)
Largest diff. peak and hole	0.216 and -0.237 e. $Å^{-3}$

Synthesis of the compound

A mixture of isatin 1 (1.0 mmol), sarcosine 2 (1.1 mmol) and (E)-2-(1H-indole-3-carbonyl)-3-(4-oxo-4H-chromen-3-yl) acrylonitrile 3 (1.1 mmol) in methanol was refluxed for 2 hour.. The solid precipitated in the reaction mixture was filtered. The resulting crude was purified by flash column chromatography (mesh 100-200) using hexane / EtOAC (7:3) and the solid single product was finally recrystallized from ethanol to obtain pure product in good yield 99%. The synthesis reaction is given below.



Results and Discussion

Single crystal X-ray analysis confirms the molecular structure and atom connectivity as illustrated in Fig. 1. The sum of the angles at N1 of the pyrrolidine ring [327.6(6) º] is in accordance with sp^2 hybridization. The five membered ring in the pyrrole and pyrrolidine (with a C atom as the flap atom) ring system adopts an envelope conformations with puckering

Parameters[8], q_2 = 0.399(3) Å, ϕ_2= 211.0(3) º and q_2 = 0.082(3) Å, ϕ_2= 243.7(17) º, respectively. The pyrrole ring makes dihedral angles of 83.9(11) and 89.35(11) º with the mean plane through all non-H atoms of the indoline and chromene ring system, respectively. The mean plane through the chromene group forms a dihedral angles 77.02(11) º with the plane of the indoline ring system. In the crystal, molecules are connected by C---H...O hydrogen-bonding interactions, which form centrosymmetric patterns described by graph-set ring motif

$R^2_2(6)$ (Fig 2 & Table 2). The crystal structure is also stablized by C---H...π interactions and by aromatic π-- π

stacking interactions. The selected bond lengths and angles are listed in table 3 and 4, respectively.

Table 2: Hydrogen-bond geometry [Å]

Distance (Å)				Angle (º)
D—H…A	D—H	H…A	D…A	D—H…A
C1—H1B…O3^{i}	0.97	2.56	3.303(3)	134

Symmetry code: i) 1-x,1-y,1-z

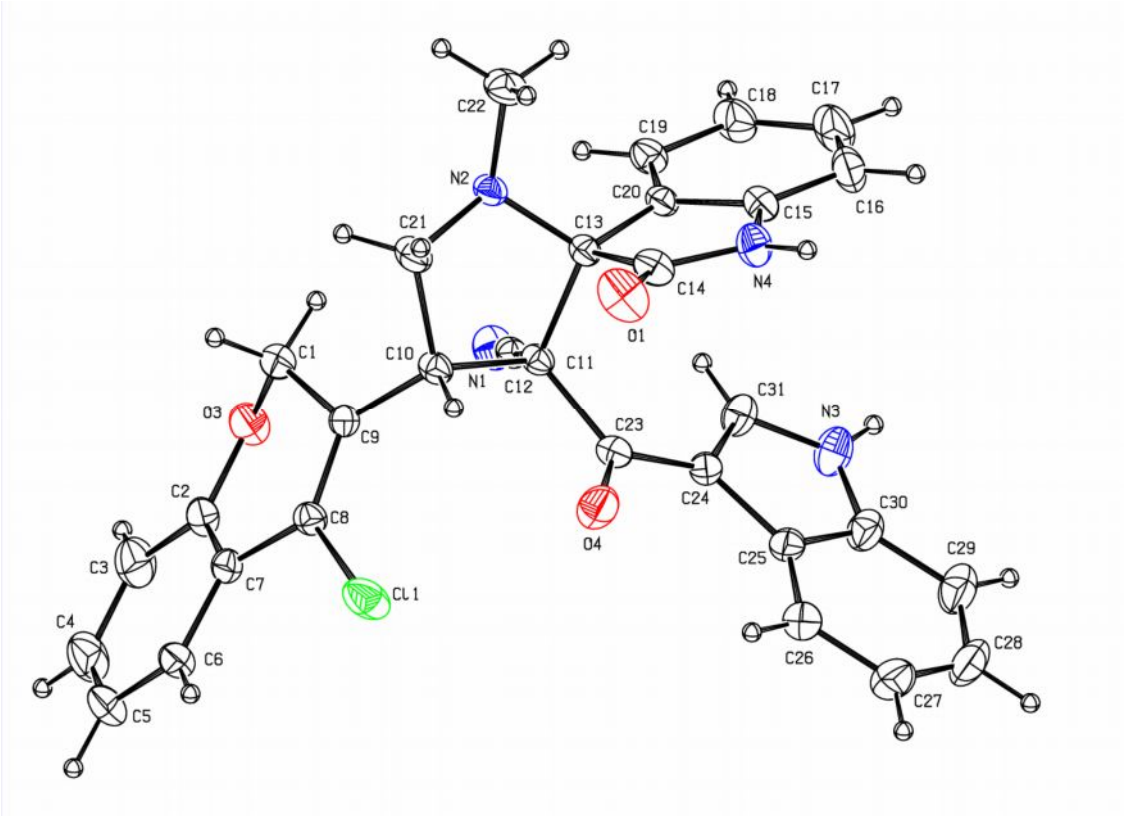


Fig 1. The molecular structure of the title compound, with atom labeling. Displacement ellipsoids are drawn at the 30% probability level.

Table 3: Selected Bond lengths (Å)

Atom	Length	Atom	Length
C(1)-C(9)	1.507(3)	C(7)-C(8)	1.463(3)
C(1)-H(1A)	0.9700	C(8)-C(9)	1.342(3)
C(1)-H(1B)	0.9700	C(8)-Cl(1)	1.722(2)
C(2)-O(3)	1.371(3)	C(9)-C(10)	1.504(3)
C(2)-C(3)	1.383(3)	C(10)-C(21)	1.543(3)
C(2)-C(7)	1.393(3)	C(10)-C(11)	1.578(3)
C(3)-C(4)	1.381(4)	C(11)-C(12)	1.465(3)

Table 4: Selected Bond angles (°)

Atom	Angle	Atom	Angle
O(3)-C(1)-C(9)	111.89(17)	C(3)-C(2)-C(7)	121.3(2)
O(3)-C(1)-H(1A)	109.2	C(4)-C(3)-C(2)	119.0(3)
C(9)-C(1)-H(1A)	109.2	C(4)-C(3)-H(3)	120.5
O(3)-C(1)-H(1B)	109.2	C(2)-C(3)-H(3)	120.5
C(9)-C(1)-H(1B)	109.2	C(5)-C(4)-C(3)	121.0(2)
H(1A)-C(1)-H(1B)	107.9	C(5)-C(4)-H(4)	119.5
O(3)-C(2)-C(3)	117.6(2)	C(3)-C(4)-H(4)	119.5
O(3)-C(2)-C(7)	121.01(19)	C(4)-C(5)-C(6)	119.5(2)

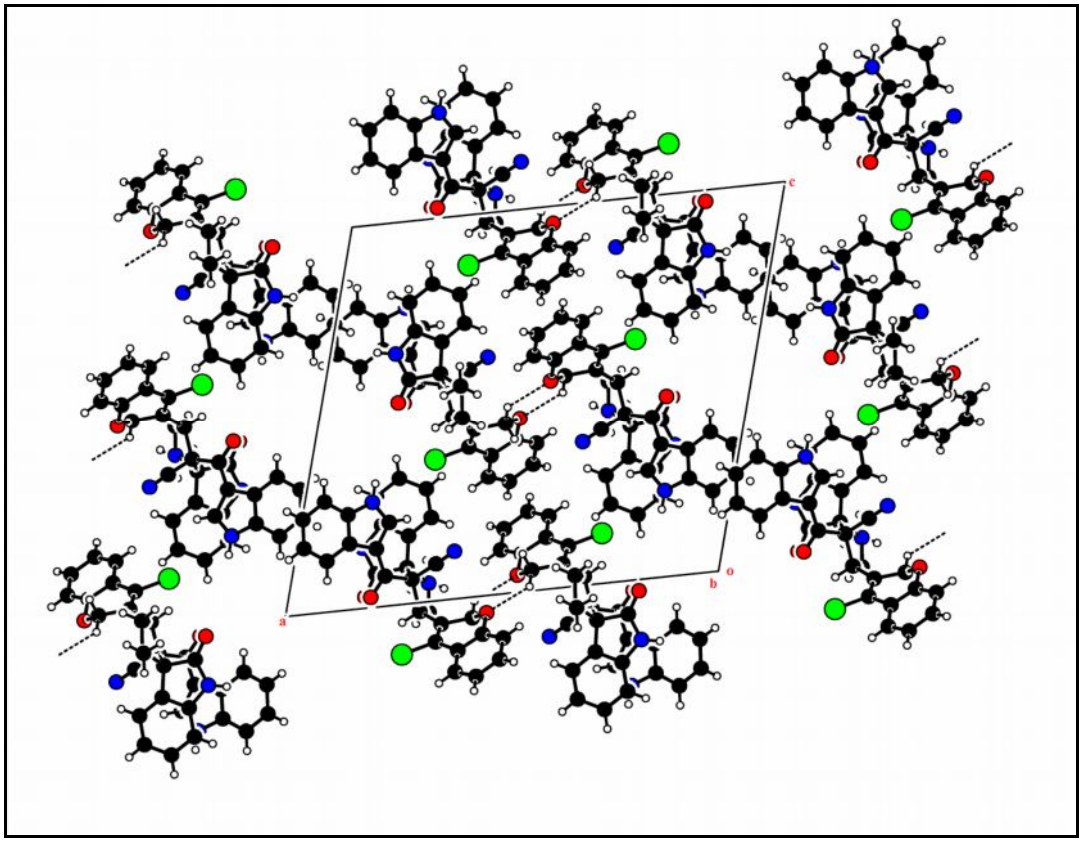


Fig 2. The crystal packing of the titled compound forming centrosymmetric patterns described by graph-set ring motif $R^2_2(6)$ viewed along c axis. The hydrogen bonds are shown as dashed lines (see Table 2 for details).

Conclusion

The crystal structure analysis of a novel Spiro pyrrolidine and Indoline compound was studied using x-ray diffraction method. In the compound, the crystal packing is stabilized by intermolecular C—H…O hydrogen bonds.

Acknowledgments

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Crystallographic data for the structure reported here have been deposited with CCDC (Deposition No's.CCDC: 1051702). These data can be obtained free of charge via http: // www . ccdc. cam. ac. uk/ conts/retrieving.html or from CCDC, 12 Union Road, Cambridge CB2 1EZ, UK,
E-mail: deposit@ccdc.cam.ac.uk.

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