Crystal Structure of Sertraline Key Intermediate: 4-(3,4-Dichlorophenyl)-3,4-dihydro-1(2H)-naphthalone, Tetralone

G. SARALA,* C. V. KAVITHA,** K. MANTELINGU,** Sridhar M. ANANDALWAR,*†
J. Shashidhara PRASAD,* and K. S. RANGAPPA**

*Department of Studies in Physics, University of Mysore, Mysore 570006, India

**Department of Studies in Chemistry, University of Mysore, Mysore 570006, India

The compound, 4-(3,4-dichlorophenyl)-3,4-dihydro-1(2H)-naphthalone (tetralone), $C_{16}H_{12}Cl_2O$, crystallizes in the monoclinic crystal class in the space group $P2_1/n$ with cell parameters $a = 10.606(2)\text{\AA}$, $b = 22.110(5)\text{\AA}$, $c = 12.477(2)\text{\AA}$, $\beta = 110.647(1)^\circ$, $V = 2737.9(9)\text{\AA}^3$ and $Z = 8$.

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Sertraline hydrochloride is a very effective antidepressant. It selectively blocks serotonin reuptake and is used for the treatment of depression, as well as dependency and other anxiety-related disorders.¹ Sertraline belongs to those medicinal agents having one or more asymmetric centers in which the isomers show significant differences in their biological activity² and therefore, it is necessary to produce the biologically active 1*S*,4*S*-enantiomer, sertraline, with high optical purity. There are a number of approaches reported for the synthesis of sertraline hydrochloride. One of them involves the synthesis of tetralone. The synthesis of tetralone, a key intermediate of sertraline is of great interest. This prompted us to conduct a molecular structure analysis of the title compound tetralone. A schematic diagram of molecule is given in Fig. 1. The synthesis of the title compound was reported earlier.³

A single crystal of suitable dimensions was chosen for an X-ray diffraction study. All of the measurements were made on a DIPLabo Imaging Plate system with graphite-monochromated Mo K_α radiation. Thirty six frames of data were collected using an oscillation method. Image processing and data reduction were done using Denzo.⁴ The structure was solved using SHELXS-97.⁵ A full-matrix least-squares refinement was performed using SHELXL-97.⁵ The R_1 value is 0.0972 for 2395 reflections (0.1256 for all 3800 reflections) with 344 parameters. Table 1 gives the experimental crystallographic

Fig. 1 Schematic diagram of the molecule.

† To whom correspondence should be addressed.
E-mail: mas@physics.uni-mysore.ac.in

data. Table 2 gives selected bond lengths and bond angles. Figure 2 gives a ORTEP drawing of the molecule at 50% probability. Figure 3 gives a packing drawing of the molecule along the b axis.

There are two molecules in the asymmetric unit. The two independent molecules have almost the same conformation. The 3,4-dihydro-1(2H)-naphthalone (ring 1) is in a nearly orthogonal position to the 4-(3,4-dichlorophenyl) (ring 2) with a dihedral angle $86.66(25)^\circ$. The 3,4-dihydro-1(2H)-naphthalone adopts a half chair conformation with atom C10A deviating from the Cremer and Pople plane⁶ defined by the atoms C11A, C12A, C13A, C14A, C15A, C16A, C17A and C18A by $-0.355(6)\text{\AA}$. The puckering coordinates (Q , θ , and ϕ) are given by $0.5080(57)\text{\AA}$, $57.53(63)^\circ$, $50.0(8)^\circ$, respectively. The bond lengths and the bond angles have normal values. The structure

Table 1 Crystal data and structure refinement

Empirical formula	$C_{16}H_{12}Cl_2O$
Formula weight	582.31
Crystal system	monoclinic
Space group	$P2_1/n$
Cell dimensions	$a = 10.606(2)\text{\AA}$ $b = 22.110(5)\text{\AA}$ $c = 12.477(2)\text{\AA}$ $\beta = 110.647(1)^\circ$
Volume	$2737.9(9)\text{\AA}^3$
Z	8
Density(calculated)	1.413 Mg/m^3
Number of reflections used	6591
$\theta_{\max}$	25.02°
Data/restraints/parameters	3800/0/344
R	0.0972
$(\Delta/\sigma)_{\max}$	0.001
$(\Delta\rho)_{\max}$	$0.976\text{ e}\text{\AA}^{-3}$
$(\Delta\rho)_{\min}$	$-0.545\text{ e}\text{\AA}^{-3}$
Measurement	DIPLabo
Program system	Denzo
Structure determination	SHELXS-97
Refinement	full-matrix: SHELXL-97
CCDC number	616505

Table 2 Selected bond lengths (Å) and bond angles (°)

Atoms	Length	Atoms	Length
C11A-C4A	1.728(5)	C11B-C4B	1.733(6)
C12A-C5A	1.716(5)	C12B-C5B	1.722(6)
C8A-C9A	1.527(6)	C8B-C9B	1.520(7)
C9A-C18A	1.521(7)	C9B-C10B	1.498(8)
C9A-C10A	1.533(7)	C9B-C18B	1.533(8)
C12A-O19A	1.214(6)	C12B-O19B	1.205(6)
C12A-C13A	1.490(7)	C12B-C13B	1.488(8)
C13A-C14A	1.393(7)	C13B-C14B	1.385(8)
C13A-C18A	1.413(6)	C13B-C18B	1.411(7)
C14A-C15A	1.364(8)	C14B-C15B	1.371(9)
C5A-C4A-C11A	120.4(4)	C5B-C4B-C11B	119.4(5)
C3A-C4A-C11A	119.1(4)	C3B-C4B-C11B	118.7(5)
C4A-C5A-C12A	121.1(4)	C4B-C5B-C12B	122.1(6)
C6A-C5A-C12A	119.6(4)	C6B-C5B-C12B	118.9(6)
C3A-C8A-C9A	119.5(4)	C3B-C8B-C9B	120.1(5)
C7A-C8A-C9A	121.8(4)	C7B-C8B-C9B	121.4(5)
C18A-C9A-C8A	113.7(4)	C10B-C9B-C8B	112.6(5)
C18A-C9A-C10A	109.5(4)	C10B-C9B-C18B	112.1(5)
C8A-C9A-C10A	111.7(4)	C8B-C9B-C18B	112.0(5)
O19A-C12A-C13A	121.2(5)	O19B-C12B-C13B	120.3(6)
O19A-C12A-C11A	120.5(5)	O19B-C12B-C11B	122.6(6)
C17A-C18A-C9A	122.4(4)	C17B-C18B-C9B	123.0(5)
C13A-C18A-C9A	119.6(4)	C13B-C18B-C9B	119.5(5)

Fig. 2 ORTEP drawing of the molecule at 50% probability.

exhibits intermolecular hydrogen bonding of the type C-H...O with a bond length of 3.318(7) Å and a bond angle of 171° with the symmetry code $-1/2 + x, 1/2 + y, 1/2 + z$. The packing of the molecules when viewed down the *b* axis indicates that the

Fig. 3 Packing drawing of the molecule along the *b* axis.

molecules are interlinked by hydrogen bonds.

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