The Crystal Structure of 4-amino-5-chloro-*N*-[2-(diethylamino)ethyl] -*o*-*anisamide* Monohydrochloride Monohydrate

Anjana Chauhan[1] and Rajendra Kumar Tiwari[2]
Associate Professor,Deptt. of ECE[1], Faculty of Engineering & Technology, MBU Solan[1],
Professor,Deptt. of Physics[2], School of Studies in Physics, Jiwaji University, Gwalior (M.P.), INDIA[2].
Email: anjuswayinn@yahoo.co.in[1], phy05@rediffmail.com[2]

Abstract- The title compound is also known as Metoclopramide hydrochloride. It is a white, crystalline, odorless substance, freely soluble in water. The crystal structure was determined from single-crystal X-ray diffraction data. It crystallizes in the Monoclinic space group $P2_1/n$ with unit cell dimensions a = 12.105(5) Å, b = 8.538(5) Å, c = 17.080(5) Å and β = 98.063(5)˚. The bond angles in the benzene ring range from 106.90(13) to 121.28(13)˚. The structure is stabilized by three intra-molecular and three intermolecular hydrogen bonds. One very close hydrogen bond is observed between O(3)-O(2) # 3 of 2.7498(18)Å in which the distance between hydrogen and acceptor is 1.822(11)Å.

Index Terms- X-Ray Diffraction, Metoclopramide, Bond Lengths

1. INTRODUCTION

Metoclopramide was first described by Dr.Louis Justin-Besançon and C. Laville in 1964.[1] It is an antiemetic and gastroprokinetic agent. It is commonly used to treat nausea and vomiting (emesis) associated with conditions including: emetogenic drugs, uraemia, radiation sickness, malignancy, labor, and infection.[2,3] Metoclopramide hydrochloride is a white, crystalline, odorless substance, freely soluble in water. Chemically, it is 4-amino-5-chloro-*N*-[2-(diethylamino)ethyl] -*o*-*anisamide* monohydrochloride monohydrate. Its molecular formula is $C_{14}H_{22}ClN_3O_2$•HCl•H_2O. Its molecular weight is 354.27. Molecular structure of title compound is shown in Figure 1.

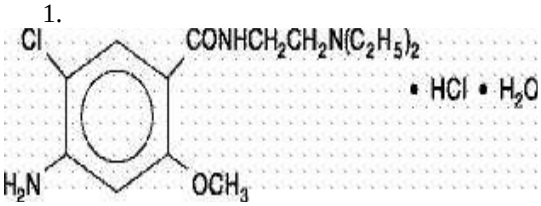

Figure 1: Molecular structure of Metoclopramide HCl

This compound has wide range biological activity. Herein we report the crystal structure of the title compound using single-crystal X-ray diffraction.

2. EXPERIMENTAL

Thin transparent crystals were obtained by slow evaporation method from a solution of acetone, at 293K. The density of the crystal was determined by floatation method in the mixture of benzene and carbon tetrachloride. The crystal was placed in RD bottle filled with carbon tetrachloride. Benzene was added to the solution until the crystal floated in the middle of mixture. Thus the crystal and solution were of same density and the density of solution was measured with pyknometer. The measured density is 1.235mg/m^3 and calculated density is 1.346mg/m^3.

X-Ray Data Collection and Structure Refinement

Experimental data are listed in Table 1. The atomic coordinates and equivalent isotropic displacement parameters for non-hydrogen atoms are reported in Table 2. The bond lengths and angles and hydrogen-bond geometry are given in Tables 3 and 4, respectively. The three dimensional intensity data were collected on a computerized automatic 4-circle CAD-4 Enraf-Nonious Diffractometer using graphite filtered CuKα radiations (λ = 1.5418Å) at T = 273 K. Absorption correction was applied. The data collection was done by a θ range of 2.22 to 29.19˚. The crystal structure was solved using SHELXS-97[4] program for crystal structure solution and refined by SHELXL-97[5] refinement program.

Table 1. Experimental Data.

Empirical formula	$C_{14}H_{25}Cl_2N_3O_3$
Formula weight	354.27
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P21/n
Unit cell dimensions	a = 12.105(5) Å , α = 90.000(5)˚ b = 8.538(5) Å , β = 98.063(5)˚ c = 17.080(5) Å, γ= 90.000(5)˚

Volume	1747.8(14) Å^3
Z, Calculated density	4, 1.346 Mg/m^3
Absorption coefficient	0.387 mm^{-1}
F(000)	752
Crystal size	0.30 x 0.20 x 0.20 mm
Theta range for data collection	2.22° to 29.19 °
Limiting indices	-14<=h<=16, -11<=k<=9, -23<=l<=20
Reflections collected / unique	21894 / 4728 [R(int) = 0.0257]
Completeness to theta = 29.19°	99.7 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.930 and 0.840
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4728 / 3 / 227
Goodness-of-fit on F^2	1.051
Final R indices [I>2sigma(I)]	R1 = 0.0368,wR2 = 0.0913
R indices (all data)	R1 = 0.0591,wR2 = 0.1024
Extinction coefficient	0.0079(10)
Largest diff. peak and hole	213 and -0.219 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2 x 10^3).

Atom	x	y	z	U(eq)
C(1)	3645(1)	2175(2)	5889(1)	61(1)
C(2)	4639(1)	3167(2)	5781(1)	46(1)
C(3)	5240(1)	3677(2)	7206(1)	49(1)
C(4)	6204(2)	3985(2)	7839(1)	63(1)
C(5)	6098(1)	1475(2)	6583(1)	47(1)
C(6)	6420(1)	681(2)	5860(1)	46(1)
C(7)	7074(1)	2076(2)	4762(1)	42(1)
C(8)	8005(1)	2812(2)	4419(1)	39(1)
C(9)	9151(1)	2710(2)	4705(1)	39(1)
C(10)	9926(1)	3478(2)	4326(1)	43(1)
C(11)	9609(1)	4410(2)	3659(1)	42(1)
C(12)	8471(1)	4481(2)	3374(1)	43(1)
C(13)	7705(1)	3705(2)	3744(1)	42(1)
C(14)	10603(1)	1634(2)	5654(1)	58(1)
N(1)	10384(1)	5189(2)	3315(1)	57(1)
N(2)	7269(1)	1492(2)	5496(1)	45(1)
N(3)	5582(1)	3059(1)	6452(1)	39(1)
O(1)	9448(1)	1807(1)	5360(1)	50(1)
O(2)	6133(1)	2016(2)	4384(1)	64(1)
O(3)	5389(1)	7643(2)	6960(1)	68(1)
Cl(1)	8027(1)	5603(1)	2539(1)	63(1)
Cl(2)	7057(1)	5762(1)	6018(1)	57(1)

Table 3. Selected bond lengths (Å) and angles (˚).

C(2)-N(3)	1.5026(18)
C(3)-N(3)	1.5029(19)
C(5)-N(3)	1.4931(19)
C(6)-N(2)	1.4492(19)
C(7)-O(2)	1.2296(17)
C(7)-N(2)	1.3379(19)
C(9)-O(1)	1.3650(17)
C(11)-N(1)	1.350(2)
C(12)-Cl(1)	1.7395(15)
C(14)-O(1)	1.4258(18)
O(2)-C(7)-N(2)	120.29(13)
O(2)-C(7)-C(8)	120.65(13)
N(2)-C(7)-C(8)	119.05(12)
O(1)-C(9)-C(10)	122.41(12)
O(1)-C(9)-C(8)	116.91(12)
N(1)-C(11)-C(12)	122.62(15)
N(1)-C(11)-C(10)	120.48(14)
C(13)-C(12)-Cl(1)	119.68(11)
C(11)-C(12)-Cl(1)	119.04(11)
C(2)-N(3)-C(3)	111.13(11)

Table 4. Hydrogen bond geometry (Å and ˚).

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DH….A)
N(1)-H(1D)...O(3)#1	0.829(18)	2.170(19)	2.965(2)	160.4(17)
N(1)-H(1E)...Cl(2)#2	0.89(2)	2.37(2)	3.250(2)	168.9(19)
N(2)-H(2C)...O(1)	0.857(18)	2.057(18)	2.6939(19)	130.4(15)
O(3)-H(3A)...O(2)#3	0.941(9)	1.822(11)	2.7498(18)	168(2)
O(3)-H(3B)...Cl(2)	0.940(9)	2.259(11)	3.1865(16)	168.7(19)
N(3)-H(3C)...Cl(2)	0.915(17)	2.172(18)	3.0716(17)	167.6(14)

Symmetry codes: #1 x+1/2,-y+3/2,z-1/2 #2 -x+2,-y+1,-z+1 #3 -x+1,-y+1,-z+1

3. RESULTS AND DISCUSSIONS

The ORTEP[6] view of the molecule with thermal ellipsoids is depicted in Figure. 2. All the bond lengths in the benzene ring vary from 1.364(2) to 1.4071(19)Å. The distances show good agreement with the standard value of 1.395 Å. The deviations of the inner bond angles in the benzene ring from 120˚are only very slightly greater than 2σ(=0.7˚). However the C(11)-N(1) bond distance of 1.350(2)Å

is significantly shorter than the accepted C-N single bond distance of 1.472Å ($\Delta > 3\sigma$). In many other cases wherever nitrogen has trigonal hybridization, the similar shortening of C-N bond has been observed. All other C-C bond lengths show normal values[7] and the C-O and C=O bond lengths are comparable to those observed in similar structures.[8-15] The bond angles in the benzene ring range from 106.90(13) to 121.28(13)˚. The molecular packing of metoclopramide seen down a- axis is shown in Figure. 3**.** It is seen in Table 4 clearly there are three intramolecular and three intermolecular hydrogen bonds. The N(1), N(2), O(3) and N(3) are hydrogen bonded to O(3) # 1, O(1), O(2) # 3 and Cl(2) respectively of the symmetry related molecules. The molecules are staged together along both the diagonals of the bc plane and crosslink each other at the center of the cell.

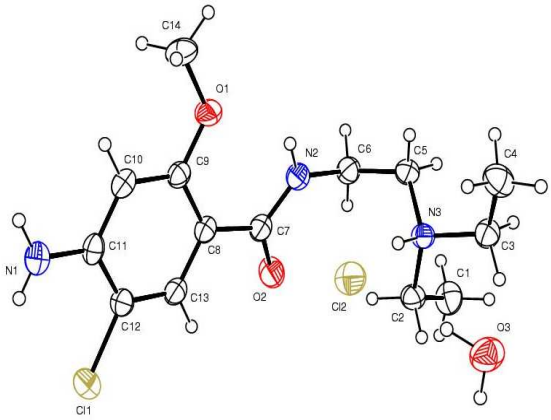

Figure 2: ORTEP view of the title compound with the atom-numbering scheme.

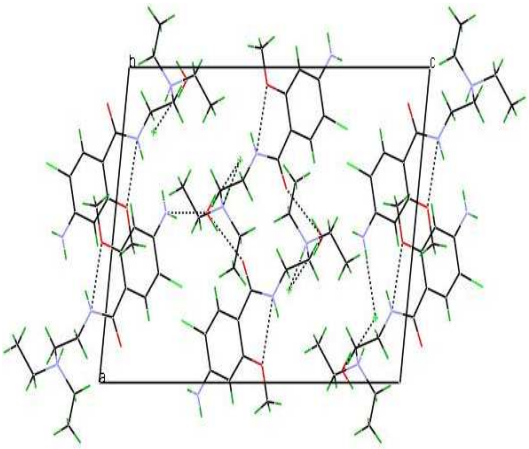

Figure 3: Molecular packing of Metoclopramide seen down a- axis.

Supplementary Material

Crystallographic data for the structure reported in this paper have been deposited at the Cambridge Crystallographic Data Centre. Copies of the data (**CCDC745580**) can be obtained free of charge upon application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [e-mail: deposit@ccdc.cam.ac.uk].

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