Chemical Analysis of $C_{10}H_{11}N_3O_3S$ - A Sulpha Drug

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Abstract: Structural analysis of medicinal compound is important for understanding of the compound and its interaction as a medicine. In the present paper, the chemical studies on Suphamethoxazole ($C_{10}H_{11}N_3O_3S$) carried out by Gaussian 09 software to determine total energy, molecular energies and atomic mass distributions and also calculate the bond lengths bond angles and torsional angles. And its structural analysis using X-ray technique has been done after growing it with slow evaporation using methanol as a solvent.

Keywords: Sulphamethoxazole, Single crystal, Medicinal compound, Slow evaporation, Crystal arrangement.

I. Introduction

Title compound is a Sulpha drugs belongs to a class of organic compounds Sulpha drugs have a wide spectrum of applications as anti-bacterial, anti-fungal, anti-malerial, and anti-cancer drugs [1-4]. They are used in the treatment of infection, especially for patients intolerant to antibiotics and therefore its study becomes a major area of research and an important branch of commercially significance in pharmaceutical sciences. Sulphamethoxazole is a bacteriostatic antibacterial agent [5]. It is used for bacterial infections such as respiratory tract infections and gastrointestinal tract infection. In present paper, reports the study of sulphamethoxazole by X-ray crystallography and DFT calculation. DFT calculations are carried out to determine bond lengths, bond angles and torsional angles of molecule by calculating the total energy of a molecule for different molecular geometries and it shows that which conformation is having lowest energy.

II. Experimental

The title compound Sulphamethoxazole has been dissolved in ethyl alcohol solution. After 10 days the colorless well formed cubic shaped crystals can be seen in the beaker. The density of crystal is measured by flotation technique using the mixture of benzene and carbon tetrachloride measured with pyknometer. Intensity data collection of title compound has been carried out at X-ray Lab, the facility of SAIF, IIT Chennai on CAD-4 diffractometer. The structure has been solved by direct method using SIR92 software programme. All of the non-hydrogen atoms have been refined anisotropically by full-matrix least-squares on F2 using SHELXL97 [6]. The intermolecular hydrogen bonding interactions and the molecular graphics were prepared using PARST and PLATON software programmes [7].

III. Computational Method

All theoretical calculation of title compound has been carried out by Gaussian 09 programme at the RHF / 6-31G** and B3LYP / 6-31G* levels. All calculations have been carried out at SAIF IIT Chennai using the default convergences criteria.

IV. Result and Discussion

The ORTEP view of title compound showing 50% probability displacement ellipsoids numbering scheme is shown in Fig. 1.

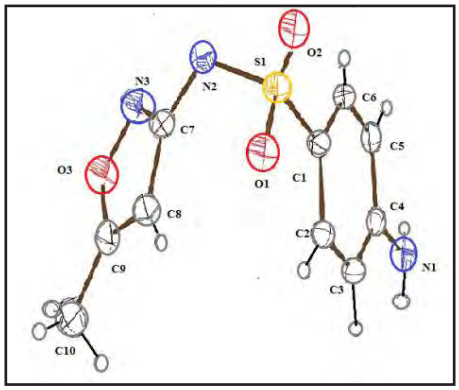

Fig. 1. ORTEP view of the Sulphametoxazole

In the structure, the benzene ring the bond lengths of C(2)-C(3) and C(5)-C(6) are the smaller than the mean value of 1.40. Further in benzene ring the bond length of C(5)-C(6) and C(2)-C(3) are shorter than the other bond lengths. All the bond angles of the benzene ring are agreed well with the standard values.

At the atom S(1) has been found tetrahedral geometry, which is found slightly distorted from the ideal tetrahedral configuration. The widening of angle O(2)- S(1)- O(1) [119.49(10)˚] and narrowing of angle N(2)-S(1)- C(1) [107.24(9)˚] from the ideal tetrahedral configuration, which is recognized to the Thorpe Ingold effect [8].

V. Molecular Geometry

The theoretical calculations carried out by RHF and B3LYP theory. The geometrical parameters bond lengths, bond angles, torsional angles are listed in Table 1, Table 2, and Table 3 respectively and compared with experimental values. From Table 2 it is seen that the biggest difference between theoretical and experimental values occurs at N(2)-S(1) bond with difference 0.0960 Å for B3LYP method and at C(4)-N(1) bond with the difference value being 0.090 Å for RHF method. In bond angles, the biggest difference between experimental and theoretical values takes place at O(2)-S(1)-O(1) with difference being 0.06˚ and 0.07˚ for B3LYP and RHF respectively. The difference between calculated and observed geometry could be related to the crystal packing in the molecules.

Table I: Camparison of Bond Lengths Obtained by RHF And B3LYP Methods With Experimental Values

Atoms	*B3LYP/ 6-31G**	*RHF/6-31G***	*Exp.*
C(1)-C(2)	1.376	1.382	1.387(3)
C(1)-C(6)	1.389	1.382	1.388(3)
C(1)-S(1)	1.750	1.747	1.746(2)
C(2)-C(3)	1.398	1.384	1.378(2)
C(3)-C(4)	1.397	1.384	1.388(3)
C(4)-N(1)	1.380	1.488	1.378(3)
C(4)-C(5)	1.393	1.398	1.390(3)
C(5)-C(6)	1.387	1.384	1.377(3)
C(7)-N(3)	1.298	1.289	1.293(3)
C(7)-C(8)	1.399	1.397	1.397(3)
C(7)-N(2)	1.410	1.405	1.404(3)
C(8)-C(9)	1.348	1.344	1.343(3)
C(9)-O(3)	1.350	1.348	1.345(3)
C(9)-C(10)	1.487	1.464	1.468(3)
N(2)-S(1)	1.740	1.646	1.6450(19)
N(3)-O(3)	1.409	1.413	1.408(3)
O(1)-S(1)	1.4451	1.4347	1.4343(15)
O(2)-S(1)	1.4380	1.4347	1.4286(15)

Table II: Camparison of Bond Angles Obtained by RHF and B3LYP Methods With Experimental Values

Atoms	*B3LYP/ 6-31G**	*RHF/6-31G***	*Exp.*
C(2)-C(1)-C(6)	120.34	120.23	120.37(19)
C(2)-C(1)-S(1)	120.45	120.43	120.40(15)
C(6)-C(1)-S(1)	119.19	119.19	119.20(15)
C(3)-C(2)-C(1)	119.56	119.45	119.59(19)
C(2)-C(3)-C(4)	120.50	120.54	120.78(19)
N(1)-C(4)-C(3)	120.62	120.57	120.8(2)
N(1)-C(4)-C(5)	120.21	120.53	120.3(2)
C(3)-C(4)-C(5)	118.92	118.89	118.89(19)
C(6)-C(5)-C(4)	121.10	121.02	121.00(19)
C(5)-C(6)-C(1)	119.30	119.37	119.35(18)
N(3)-C(7)-C(8)	112.50	112.35	112.7(2)
N(3)-C(7)-N(2)	118.32	118.28	118.24(19)
C(8)-C(7)-N(2)	129.30	129.18	129.02(19)
C(9)-C(8)-C(7)	104.62	104.63	104.60(19)
C(8)-C(9)-O(3)	109.4	109.4	109.2(2)
C(8)-C(9)-C(10)	133.7	133.8	133.9(2)
O(3)-C(9)-C(10)	116.7	116.6	116.9(2)
O(2)-S(1)-O(1)	119.55	119.56	119.49(10)
O(2)-S(1)-N(2)	107.55	107.56	107.54(10)
O(1)-S(1)-N(2)	104.12	104.10	104.06(10)
O(2)-S(1)-C(1)	108.37	108.31	108.35(9)
O(1)-S(1)-C(1)	109.50	109.48	109.49(9)
N(2)-S(1)-C(1)	107.25	107.23	107.24(9)
C(7)-N(2)-S(1)	120.58	120.52	120.54(14)
C(7)-N(3)-O(3)	104.75	104.73	104.71(18)
C(9)-O(3)-N(3)	108.70	108.73	108.72(17)

Table III: Camparison Of Torsional Angles Obtained By RHF And B3LYP Methods With Experimental Values

Atoms	*B3LYP/ 6-31G**	*RHF/6-31G***	*Exp.*
C(6)-C(1)-C(2)-C(3)	2.3	1.6	1.4(3)
S(1)-C(1)-C(2)-C(3)	180.32	170.32	179.36(15)
C(1)-C(2)-C(3)-C(4)	-2.2	-1.9	-1.1(3)
C(2)-C(3)-C(4)-N(1)	184.4	180.3	177.2(2)
C(2)-C(3)-C(4)-C(5)	0.4	0.8	0.2(3)
N(1)-C(4)-C(5)-C(6)	-185.34	-186.45	- 176.61(19)
C(3)-C(4)-C(5)-C(6)	1.3	1.5	0.4(3)
C(4)-C(5)-C(6)-C(1)	-0.8	-0.9	-0.1(3)
C(2)-C(1)-C(6)-C(5)	-1.3	-1.5	-0.8(3)
S(1)-C(1)-C(6)-C(5)	-190.45	-195.54	-178.82(15)
N(3)-C(7)-C(8)-C(9)	-1.4	-1.6	-0.8(3)
N(2)-C(7)-N(3)-O(3)	-194.04	-187.04	-177.03(17)
C(8)-C(9)-O(3)-N(3)	1.1	1.4	0.7(3)
C(10)-C(9)-O(3)-N(3)	182.6	186.04	179.8(2)
C(7)-N(3)-O(3)-C(9)	-2.1	-1.8	-1.2(3)
C(7)-N(2)-S(1)-O(2)	-65.43	-62.54	-59.45(18)
C(7)-N(2)-S(1)-O(1)	182.65	190.34	172.86(16)
C(7)-N(2)-S(1)-C(1)	65.32	67.33	56.89(18)
C(2)-C(1)-S(1)-O(2)	16.34	15.24	14.21(19)
C(6)-C(1)-S(1)-O(2)	-174.65	-175.54	-167.77(15)
C(2)-C(2)-S(1)-O(1)	156.04	158.06	146.09(17)
C(6)-C(1)-S(1)-O(1)	-54.95	-45.76	-35.89(18)
C(2)-C(1)-S(1)-N(2)	-110.46	-106.63	-101.60(17)
C(6)-C(1)-S(1)-N(2)	80.02	78.34	76.42(17)

References

[1] E. E. Badr, "Novel sulfanilamide as potent surfactants and antibacterial agents," *Journal of Dispersion Science and Technology*, vol. 29, no. 8, pp. 1143-1149, 2008.

[2] A. Hanafy, J. Uno, H. Mitani, Y. Kang, and Y. Mikami, "In vitro antifungal activities of sulfa drugs against clinical isolates of Aspergillus and Cryptococcus species," *Japanese Journal of Medical Mycology,* vol. 48, pp. 47-50, 2007.

[3] C. T. Supuran, A. Casini, and A. Scozzafava, "Protease inhibitors of the sulfonamide type: Anticancer, antiinflammatory, and antiviral agents," *Medicinal Research Reviews,* vol. 23, pp. 535-558, 2003.

[4] G. A. Gale, K. Kirtikara, P. Pittayakhajonwut, S. Sivichai, Y. Thebtaranonth, C. Thongpanchang, and V. Vichai, "In search of cyclooxygenase inhibitors, anti-mycobacterium tuberculosis and anti-malarial drugs from Thai flora and microbes," *Pharmacology and Therapeutics,* vol. 115, pp. 307-351, 2007.

[5] "Sulfonamides and sulfonamide combinations: Antibacterial agents," *Merck Veterinary Manual.*

[6] G. M. Sheldrick, "A short history of SHELX," *Acta Crystallographica,* vol. A64, no. 1, pp. 112-122, 2008.

[7] A. L. Spek, "Structure validation in chemical crystallography," *Acta Crystallographica,* vol. D65, pp. 148-155, 2009.

[8] A. Bassindale, *The Third Dimension in Organic Chemistry,* New York, John Wiley and Sons, 1984, ch. 1.