

EXPERIMENTAL AND THEORETICAL COMPARATIVE STUDIES OF 2-nitro 2-phenoxyate propane1,3-diol

T. Bhaskar^{1*} & N. Banumathi²

^{1,2}Rani Anna Govt. College for Women, Tirunelveli-8

Affiliated to Manonmaniam Sundaranar University, Tirunelveli-12

Abstract:

The synthesised compound a bronopol derivative, 2-nitro 2-phenoxyate propane-1,3-diol from bronopol is experimentally characterised by FTIR, ¹H NMR and ¹³C NMR spectroscopic techniques. The compound is comparatively studied theoretically using density functional theories that are in good agreement with each other.

Keywords: Bronopol derivative, IR, NMR, density functional theory

Introduction:

Bronopol is used as a preservative in various cosmetic, toiletry and household preparations particularly because of its high activity against Gram-negative bacteria, especially *Pseudomonas aeruginosa* and other pseudomonads. These organisms are common residents in water and as such can cause contamination and spoilage problems in cosmetics and toiletries [1-4]. Pseudomonads are frequently implicated, particularly in oil-in-water emulsions which contain a significant number of non-ionic surfactants [5,3,6]. Bronopol can also be used as an active agent, for example, in aerosol formulations. Bronopol has been reported to show persistent activity on the skin by Marples and Kilgman [7], this contrasts with the fact that in vitro it has been shown to have a weak growth inhibitory effect on cultured human skin cells by Onoda and Saito [8]. The density functional theory is a popular method for the calculation of molecular structures, vibrational frequencies and energies of molecules. The DFT calculations with a hybrid exchange-correlation functional B3LYP (Becke's three parameter (B3) exchange in conjunction with the Lee-Yang-Parr's (LYP) functional) have been proved to be very effective and show better agreement with the experimental values of structural characteristics of pyridine and its derivatives than the calculations containing the gradient corrected exchange functional. (9). The present work deals with the experimental and theoretical comparative studies of 2-nitro 2-phenoxyate propane1,3-diol using density functional theory.

Materials and Methods:

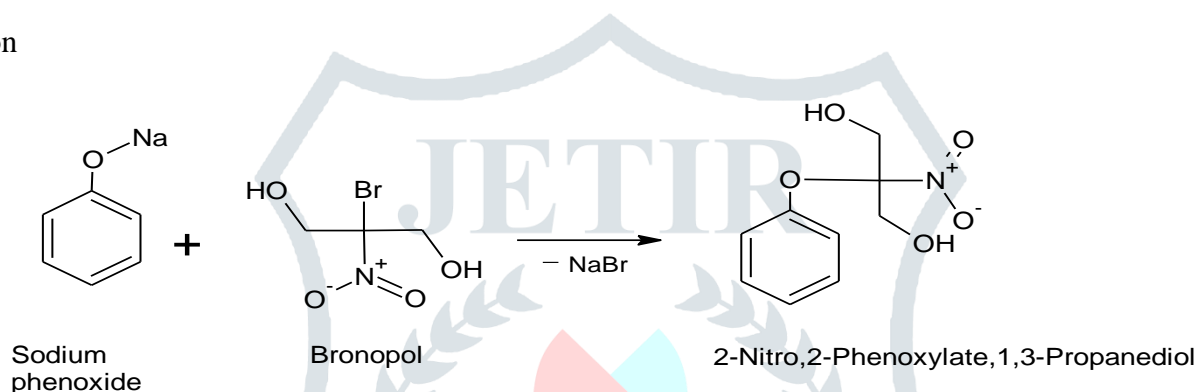
FTIR-4700 spectrometer is used for IR spectra. NMR spectra is measured from Bruker, 400 MHz Narrow Bore FT-NMR Spectrometer. All computational studies are carried out at density functional theory (DFT) level on a personal computer using Gaussian 03W program package [16] with the Becke's three-

parameter exchange functional with the LYP correction (B3LYP) and the basis set 6-31G(d,p) are used in appropriate calculations [17].

Experimental section:

0.01mol solution of sodium phenoxide is taken in a 100ml beaker in alcohol. 0.01mol of bronopol is added to it and stirred well for about 15 minutes. The reaction mixture is run by TLC, (using hexane and ethyl acetate in 3:7 ratio). No spots are formed. Then the yellow solution is kept aside in room temperature for one day. The yellow colour changes to brown colour. Then the reaction is run by TLC (using hexane and ethyl acetate in the 3:7 ratio). The formation of the product is confirmed by the appearance of the spots. Then, it is transferred to a separating funnel, by dissolving in 30 mL of ether. The organic layer is separated out in a 100ml beaker. The ether is evaporated. The 80% yield of the product obtained is in the form of solution.

Reaction



Result and Discussion:

DFT Studies:

Conformational analysis:

The geometry of 2-nitro,2-phenoxyate, propane1,3-diol is subjected to geometry optimization using B3LYP/6-31G(d,p) basis set. The numbering adopted for 2-nitro,2-phenoxyate, propane1,3-diol is shown in **Fig.1**. From the energy derived from the output file, it is concluded that the molecule with minimum energy - 780.34 a.u. is the ground state minimum energy conformer of the molecule and the selected parameters of bond length, bond angle and torsional angle of the optimized structure are presented in **Table.1**.

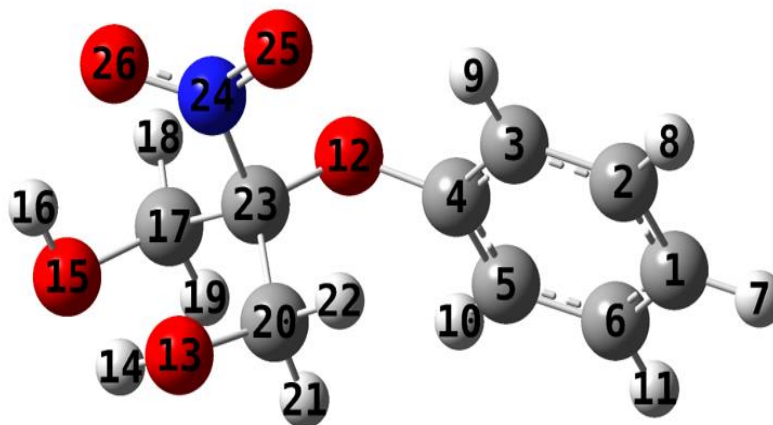


Fig.1. Numbering adopted for DFT study of 2-nitro 2-phenoxypropane 1,3-diol.

Table.1. Selected geometric parameters of 2-nitro 2-phenoxypropane 1,3-diol computed by DFT method (B3LYP/6-31G(d,p)).

Bond	Bond length (Å)	Bonds	Bond angle (°)	Bonds	Torsion angle (°)
C4-O12	1.40	C4-O12-C23	122.46	C4-O12-C23-C17	-137.16
O12-C23	1.39	O12-C23-C17	105.68	O12-C23-C17-O15	179.68
C23-C20	1.54	C23-C17-O15	114.36	O12-C23-N24-O25	-53.15
C20-O13	1.41	O12-C23-C20	116.03	O12-C23-N24-O26	126.93
C23-N24	1.58	C23-C20-O13	112.03	O12-C23-C20-O13	173.26
N24-O25	1.22	O12-C23-N24	106.82	C4-O12-C23-C20	-10.30
N24-O26	1.23	C23-N24-O25	117.29	C4-O12-C23-N24	107.42
C23-C17	1.54	C23-N24-O26	118.00	O13-C20-C23-N24	55.00
C17-O15	1.42	C17-C23-C20	113.59	-	-
-	-	C17-C23-N24	108.50	-	-

IR Vibrational Wavenumber Analysis:

The optimized geometry of 2-nitro 2-phenoxypropane 1,3-diol is subjected to IR spectral analysis using DFT method with 6-31G(d,p) basis set. It consists of 26 atoms and has 72 normal modes of vibrations which includes 25 stretching, 24 bending, 23 torsion and 27 CH stretching modes of vibration. All the modes are IR active. The molecule belongs to C₁ symmetry. There is no negative frequency observed in the DFT vibrational frequency computation which further confirmed that this optimized geometry is the ground state conformer of 2-nitro 2-phenoxypropane 1,3-diol. The experimental and predicted IR spectrum of the compound is given in **Table 2**. They are found to be in good agreement with each other.

Table 2. Significant Vibrational wavenumber obtained for 2-nitro 2-phenoxyate propane 1,3-diol at B3LYP/6-31G(d,p) level of calculations.

Mode No.	Theoretical frequencies (cm ⁻¹) DFT/B3LYP/6-31G(d,p)		Observed frequencies (cm ⁻¹)	Vibrational assignments PED≥10%
	Unscaled frequencies	Scaled frequency scaling factor = 0.9614		
72	3746	3601	3477	VO15H16(97%)
71	3697	3554		VO13H14(97%)
68	3206	3082	3438	VC1H7(31%); VC2H8(21%); VC5H10(46%)
64	3123	3002	3163	VC17H18(19%); VC17H19(80%)
63	3057	2938		VC17H18(80%); VC17H19(19%)
61	1667	1602	1631	VO25N24(58%); VO26N24(35%)

v – stretching vibration; β – bending vibration; τ – torsion bending.

¹H and ¹³C NMR Chemical-Shift Calculations:

The GIAO ¹H and ¹³C NMR chemical shift computations of 2-nitro 2-phenoxyate propane 1,3-diol is made in CDCl₃ [scrf= (solvent=chloroform)] by utilizing B3LYP/6-31G (d,p) basis set. The computational and experimental ¹H and ¹³C NMR chemical shift of the compound computed by DFT technique are displayed in

Table 3.

Table 3. ¹H and ¹³C NMR Chemical Shift computed by B3LYP/6-31G(d,p) GIAO DFT method:

Protons	Chemical shifts	Observed chemical shifts	Carbon	Chemical shifts	Observed Chemical shifts
H9	8.6	7.9-8.5	C23	176.7	173.2
H8	7.9		C4	161.7	150.5
H11	7.8		C2	135.7	120.8-132.2
H7	7.8		C6	135.0	
H10	7.5		C1	132.4	
H18	4.8	3.29-3.32	C3	130.3	79.1-79.7
H19	4.3		C5	128.8	
H21	4.2		C17	74.2	
H22	4.0		C20	71.8	
H16	3.7		-	-	-
H14	3.6		-	-	-

Polarizability calculation:

The computed values of the dipole moment (μ), the polarizability (α_0) and first hyperpolarizability (β_{tot}) by limited field approach are given in **Table 4** along with the corresponding components. 2-nitro 2-phenoxyate propane 1,3-diol is found to be polar molecule having non – zero dipole moment components. The polarizability values are dominated by the diagonal components. Hence in the presence of external fields the delocalization of the charges is expected to occur in the direction of the diagonal components.

Table.4.The electric dipole moment μ (D), the mean polarizability $\langle\alpha\rangle$ ($\times 10^{-24}$ esu) and the First hyperpolarizability β_{tot} ($\times 10^{-33}$ esu) of 2-Nitro,2-phenoxyate, propane 1,3-diol by DFT method.

Parameter	Value	Parameter	Value
μ_x	1.03	β_{xxx}	171.64
μ_y	-0.93	β_{xxy}	-6.99
μ_z	-0.24	β_{xyy}	29.33
μ	1.41	B_{yyy}	-69.41
α_{xx}	153.94	β_{xxz}	53.12
α_{xy}	0.94	β_{xyz}	6.56
α_{yy}	114.25	B_{yyz}	-5.17
α_{xz}	13.48	β_{xzz}	7.25
α_{yz}	7.57	B_{yzz}	5.61
α_{zz}	70.66	β_{zzz}	-26.57
A	112.95	β_{tot}	220.96

α : 1a.u = 0.1482×10^{-24} esu

β : 1a.u = 8.6393×10^{-33} esu

Natural Bond Order analysis:

The natural bond orbital (NBO) examination of the compound is performed at B3LYP/6 – 31G (d, p) level of calculation. The donor bonding orbitals (BD), the acceptor antibonding orbitals (BD*), the donor lone pair atoms (LP) are given in **Table 5** along with the E(2) values which assesses the interaction between the donor (filled) and acceptor (vacant) orbitals. The E (2) energy is the lowering energy that occurs during the hyperconjugative electron transfer process and thus E (2) can be referred to as stabilization energy. Larger the E(2) values, greater is the stability of the molecule.

Table.5.Second order perturbation theory analysis of fock matrix in NBO basis for 2-Nitro,2-phenoxyate, propane 1,3-diol.

Donor NBO	Occupancy	Acceptor NBO	Occupancy	E(2) in kcal/mol
(σ) C1-C2	3.64	(σ^*) C3-C4	0.39	20.64
(σ) C1-C2	3.64	(σ^*) C5-C6	0.35	21.55
(σ) C3-C4	3.64	(σ^*) C1-C2	0.34	19.64
(σ) C3-C4	3.64	(σ^*) C5-C6	0.35	19.93
(σ) C5-C6	3.64	(σ^*) C4-O12	0.03	4.45
(σ) C5-C6	3.64	(σ^*) C1-C2	0.34	19.24
(σ) C5-C6	3.64	(σ^*) C3-C4	0.39	21.56
(σ) O13-H14	1.99	(σ^*) C20-H22	0.02	2.62
(σ) O13-C20	1.99	(σ^*) O12-C23	0.04	2.21
(σ) O15-H16	1.99	(σ^*) C17-H19	0.02	2.58
(σ) C17-H18	1.98	(σ^*) C20-C23	0.05	3.36
(σ) C17-H19	1.97	(σ^*) C23-N24	0.18	5.13
(σ) C17-H19	1.97	(σ^*) O15-H16	0.02	2.37
(σ) C17-C23	1.98	(σ^*) C4-O12	0.03	2.52
(σ) C17-C23	1.98	(σ^*) N24-O25	0.60	2.27
(σ) C20-H21	1.98	(σ^*) C23-N24	0.18	4.59
(σ) C20-H22	1.98	(σ^*) O13-H14	0.03	2.50
(σ) C20-H22	1.98	(σ^*) C17-C23	0.05	3.34
(LP) O12	1.93	(σ^*) C3-C4	0.39	6.14
(LP) O12	1.93	(σ^*) C4-C5	0.03	5.63
(LP) O13	1.97	(σ^*) C3-C4	0.39	4.51
(LP) O13	1.97	(σ^*) C20-H21	0.03	6.49
(LP) O13	1.97	(σ^*) C20-C23	0.05	8.14
(LP) O15	1.97	(σ^*) O13-H14	0.03	7.96
(LP) O15	1.97	(σ^*) C17-H18	0.02	5.94

(LP) O15	1.97	(σ^*) C17-C23	0.05	6.28
(LP) O25	1.97	(σ^*) C23-N24	0.18	14.25
(LP) O25	1.97	(σ^*) N24-O26	0.06	20.28
(LP) O26	1.97	(σ^*) C23-N24	0.18	12.24
(LP) O26	1.97	(σ^*) N24-O25	0.06	19.37

Molecular Electrostatic Potential (MEP) Surface:

The reactive behaviour of the molecule is visualized with the help of three-dimensional MEP surface. The MEP surface is a superimposition of the electrostatic potential on the isoelectron density surface. MEP surface describes the charge distribution in the molecule and helps in predicting the sites for nucleophilic and electrophilic attack in the molecule. The MEP surface has been plotted for the molecule in **Fig.2**. Region of negative charge is pictured out in red colour and the red colour region is to electrophilic attack. The blue colour region represents strong positive region and is prone to nucleophilic attack. The green colour region corresponds to a potential half way between the two extremes red and blue region. The MEP diagram of the compound under study is picturised in the range of $-4.417e-3$ (red) to $+4.417e-3$ (blue) units.

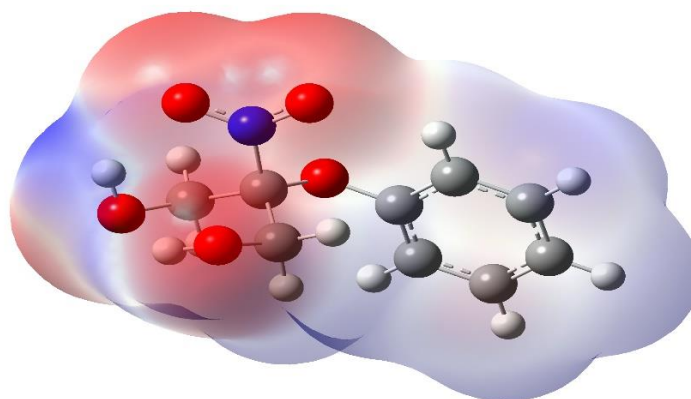


Fig.2. MEP surface of 2-nitro 2-phenoxypropane 1,3-diol.

Frontier Molecular orbital energy Calculation:

HOMO, LUMO energies and the band gap are calculated at B3LYP/6-31G(d,p) level of computation. HOMO and LUMO images of the molecule are presented in **Fig.3** and **Fig.4**. The HOMO energy, LUMO energy and band gap of the molecule are -6.9eV , -2.2eV and 4.7eV respectively. The p_z orbitals of all C, O, N atoms in the molecule participate in the HOMO orbital of the molecule. Mostly, the p_z orbitals of all moiety participate in the LUMO formation except benzene ring. The p_z orbitals of N24 and O26 participate in the HOMO formation in a very minute level.

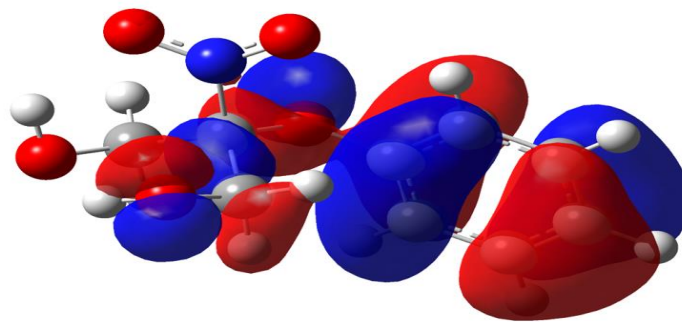


Fig.3. HOMO image of 2-nitro 2-phenoxypropane 1,3-diol.

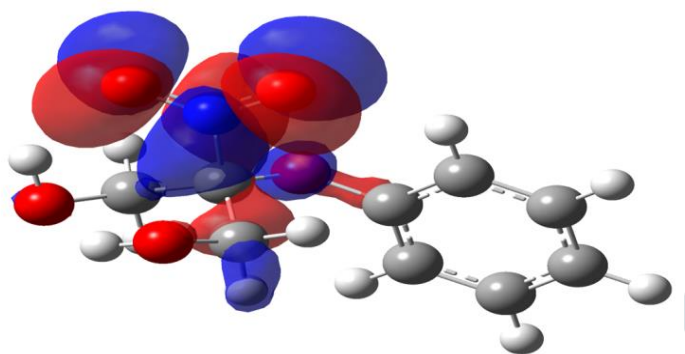


Fig.4. LUMO image of 2-nitro,2-phenoxypropane 1,3-diol.

Conclusion:

In the present research work the synthesized bronopol derivative, 2-nitro 2-phenoxypropane 1,3-diol from bronopol has been characterized by FT-IR and NMR spectroscopies. The DFT studies is carried out and compared with experimental values which are found to be good agreement with each other.

References:

- [1] L.J. Morse and L.E. Schonobock, "Hand lotions, a potential nosocomial hazard", *New England Journal of Medicine*, 278 (7), 1968, 376-378, <https://doi.org/10.1056/nejm196802152780706>
- [2] G. Sykes and R. Smart, "Preservation of preparations for application to the skin", *Am. Perfum. Cosmet.*, 88, 1969, 45.
- [3] R. Smart and D.F. Spooner, "Microbiological spoilage in pharmaceuticals and cosmetics", *J. Soc. Cosmet. Chem.*, 23, 1972, 721-737, <https://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.533.8331&rep=rep1&type=pdf>
- [4] S. Malcolm and R.C.S. Woodroffe, "The relationship between water-borne bacteria and shampoo spoilage", *J. Soc. Cosmet. Chem.*, 26, 1975, 277.
- [5] S. Tenenbaum, "The significance of pseudomonads in cosmetic products", *Am. Perfum. Cosmet.*, 86, 1971, 47.
- [6] M.J. Thomas and P.A. Majors, "Animal and human microbiological safety testing of cosmetic products", *J. Soc. Cosmet. Chem.*, 24, 1973, 135.

- [7] R.R. Marples and A.M. Kligman, "Methods for evaluating topical antibacterial agents on human skin", *Antimicrobial Agents and Chemotherapy*, 5 (3), 1974, 323-329, <https://dx.doi.org/10.1128%2Faac.5.3.323>
- [8] T. Onoda and H. Saito, "Influence of a new antibacterial agent, Bronopol, upon the growth of cultured cells", *Chemotherapy (Tokyo)*, 22, 1974, 196.
- [9] Becke, AD 1988, 'Density-functional exchange-energy approximation with correct asymptotic behaviour', *Physical Review A*, vol. 38, no. 6, pp. 3098-3100.
- [16] N. Subramanian, N. Sundaraganesan, J. Jayabharathi, *Spectrochim. Acta Part A* 76(2010) 259-269.
- [17] P. Vijaya, K.R. Sankaran, *Spectrochimica Acta Part A* 138 (2015) 460-473, <http://dx.doi.org/10.1016/j.saa.2014.11.047>.

