# Synthesis, Characterization and DFT study of 2- amino-2 (diphenylamino)- propane-1,3-diol Bhaskar T.\*, Gana Saraswathy D., Banumathi N. and Vijaya

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#### Abstract

Several attempts were made to synthesize 2- amino-2 (*diphenylamino*)-propane-1,3-diol from 2-amino-2`bromo-1,3-propane diol. This compound has been prepared by treatment of 2-amino-2`bromo-propane-1, 3 diol with diphenvlamine in alcohol and then heated for 3hrs. Yellowish brown solid was obtained. The structure of the compound was characterized by <sup>13</sup>CNMR and IR spectroscopy.

Keywords: 2-amino-2`bromo-1,3-propanediol, 2-amino-2'(diphenylamino)-1,3-propane diol, ether, alcohol and ethyl acetate.

# Introduction

Bronopol is a highly active antimicrobial compound whose chemical formula is 2-bromo-2-nitropropane 1, 3-diol. Bronopol is a white crystalline solid with strong odour. Bronopol is readily soluble in polar solvents but having less affinity in polar organic solvents. Bronopol is used in consumer products as an effective preservative agent as well as in a wide variety of industrial applications as an antimicrobial in cosmetics, external medicaments, shampoos and bath preparations. It is also used as a substitute for formaldehyde in chemical toilets.

Bronopol has a broad spectrum of antibacterial activity and is widely used at concentrations of upto 0.1% (w/v), as a preservative for pharmaceutical and cosmetic products.<sup>3,5,7,10,12,15,19</sup> The trade name of bronopol is myacide B10 and myacide AS. Among pesticides, it is categorized as bactericide. Bronopol is stable to hydrolysis under normal conditions. However, at warmer temperature and/or higher pH, it is unstable. Under these conditions, hydrolysis and degradation gave products which include formaldehyde etc.16

It causes irreversible eye damage and skin burns. It may be fatal if swallowed or inhaled and harmful if absorbed through the skin. Metabolism studies indicate that bronopol is primarily excreted in the urine<sup>2,9</sup>. The use of bronopol in personal care products (cosmetic, toiletries) has been declined since the late 1980s due to the recognized potential for nitrosamine formation.

Different instrumental methods like HPLC<sup>5,13</sup>, UVspectrophotometry<sup>8</sup>, liquid chromatography, reversed-Phase ion-pair chromatography<sup>4</sup>, enzymic micro determination<sup>14</sup> etc. are used for its determination<sup>5,19</sup>. The determination of most of the pesticides containing nitro group is based on reduction of nitro group into amino group and then subsequent diazotization and coupling with suitable reagents to form an azo dye reported<sup>1,11</sup>. The nitro group of bronopol is reduced with Zn/HCl to form amino bronopol<sup>6,17</sup>, which are subsequently diazotized and coupled with phloroglucinol to form an orange-colored azo dye in alkaline medium. The dye showed an absorbance maxima at 425nm and obeyed Beer's law in the range 10-50 µg in 1mL. The method has been successfully applied to the determination of bronopol in polluted water, grains and vegetables.

All computational studies of 2- amino-2<sup>(diphenylamino)-</sup> propane-1,3-diol from 2-amino-2`bromo-1,3-propane diol are carried out at density functional theory (DFT) level on a personal computer using Gaussian 03 W program package<sup>17</sup>. The calculations are carried out with the Becke's threeparameter exchange functional with the LYP correction (B3LYP) and the basis set 6-31G (d,p) is used in appropriate calculations. The theoretical IR vibrational frequencies are interpreted by means of potential energy distribution (PED%) calculation using vibrational energy distribution analysis (VEDA) program<sup>18</sup>.

# **Material and Methods**

A.R. grade chemicals have been used for synthesis of 2amino-2'bromo-propane-1,3-diol. TLC 60F254 pre coated plates were used and the spots were rendered visible by exposing iodine vapor. FTIR-4700 spectra were used for IR spectra. NMR and C<sup>13</sup> NMR spectra were measured from Brucker, 400 MHz Narrow Bore FT-NMR Spectrometer.

Experiment: 0.01mol of diphenylamine was taken in a 100ml round bottom flask and dissolved in ethanol. About 0.01mol of 2-Amino-2'-Bromo- 1,3-Propanediol was added to it and then it was refluxed for 3 hours and it was shaken occasionally. The product obtained is a yellowish brown precipitate. The reaction mixture was run by TLC (using hexane and ethyl acetate in the 4:6 ratio). Clear spots were obtained and were analyzed. A good yield of 70% was obtained.

A piece of a readymade silica TLC 60F254 sheet was taken. The product and reactants were spotted using a capillary tube. Then it was placed in a solvent mixture chamber. Hexane and ethyl acetate in 4:6 ratio were used as an eluent. The sheet was dried and sprayed by potassium permanganate.

Clear yellow color spots were obtained. The R<sub>f</sub> value was calculated. It confirms the formation of product, 2-amino-2<sup>(diphenylamino)-1,3-propane diol.</sup>

Fig. 1: Numbering adopted for DFT study of 2- amino-2`(diphenylamino)-Propane-1,3-diol from 2-amino-2`bromo-1,3-propane diol

 Table 1

 Selected geometric parameters of 2- amino-2`(diphenylamino)-Propane-1,3-diol from 2-amino-2`bromo-1,3-propane diol computed by DFT method (B3LYP/6-31G(d,p)).

Bond	Rond length	Ronds	Bond	Bonds	Torsion
Donu	(A <sup>o</sup> )	Donus	angle (°)	Donus	angle (°)
C1-C2	1.54	C16-N11-C27	116.12	C2-C1-N11-C16	81.1
C1-C5	1.55	C1-N11-C27	122.64	C2-C1-N11-C27	-113.6
C1-N8	1.45	C1-N11-C16	119.71	N11-C1-C2-O14	56.9
C1-O14	1.42	N8-C1-N11	112.84	O12-C5-C1-N8	52.5
C5-O12	1.42	C5-C1-N11	112.86	O12-C5-C1-C2	168.8
C1-N11	1.52	C5-C1-N8	105.92	C5-C1-C2-O14	179.4
N11-C27	1.43	C2-C1-N11	108.42	N8-C1-C2-O14	-66.1
N11-C16	1.44	O12-C5-C1	112.62	N8-C1-N11-C16	-158.3
		C5-C1-C2	107.84	C5-C1-N11-C27	126.9
		N8-C1-C2	108.78	N8-C1-N11-C27	6.9
		C1-C2-O14	112.46	C5-C1-N11-C16	-38.3

**Spectral evidences:** FTIR frequencies at 3421<sup>-1</sup>cm, 2926.62cm<sup>-1</sup> and 2855.66cm<sup>-1</sup> were obtained.

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H1NMR CH<sub>2</sub>O at  $\delta$  3.17 having 4 protons, OH at  $\delta$  1.6 is having 2 protons. Aromatic protons  $\delta$  7.31-8.31 and -NH<sub>2</sub> protons at  $\delta$  5.08 broad peak were observed. C<sup>13</sup>NMR

#### **Results and Discussion**

carbon at 53.83 ppm.

The FTIR spectrum of absorption maximum at 3421.21cm<sup>-1</sup> having a merged broad peak implies the presence of –OH

showed an aromatic carbon at 126-139 ppm and CH<sub>2</sub>O

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and  $-NH_2$  functional groups with high concentration. Peaks at 2926.62cm<sup>-1</sup> and 2855.66cm<sup>-1</sup> indicate the presence of -C-H stretching of aromatic compound. <sup>1</sup>H NMR of -CH<sub>2</sub>O peak at  $\delta$  3.17 is having 4 protons, -OH at  $\delta$  1.6 having 2 protons. Aromatic protons at  $\delta$  7.31-8.31 and -NH<sub>2</sub> protons at  $\delta$  5.08 were observed. C<sup>13</sup>NMR shows an aromatic carbon at 126-139 ppm and -CH<sub>2</sub>O carbon at 53.83ppm.

#### **Computational DFT analysis**

**Conformational Analysis:** The numbering adopted for 2amino-2`(diphenylamino)-propane-1,3-diol from 2-amino-2`bromo-1,3-propane diol in this DFT study is given in fig. 1. The molecule is designed and subjected to optimization using B3LYP/6-31G(d.p) basis set. From the energy derived from the output file, it is concluded that the molecule with minimum energy -842.374 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. The compound is subjected to further computational analysis.

**IR Vibrational Wavenumber Analysis:** The optimized geometry of 2- amino-2`(diphenylamino)-Propane-1,3-diol from 2-amino-2`bromo-1,3-propane diol is subjected to IR spectral analysis using DFT method with 6-31G(d,p) basis set. It consists of 37 atoms and has 105 normal modes of vibrations which include 36 stretching, 35 bending, 34 torsion and 42 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 confirms that this optimized geometry is the ground state conformer of 2- amino-2`(diphenylamino)-propane-1,3-diol from 2-amino-2`bromo-1,3-propane diol. The experimental and predicted IR spectrum of the compound are given in table 2. They are found to be in good agreement with each other.

<sup>1</sup>H and <sup>13</sup>C NMR Chemical-Shift Calculations: The GIAO <sup>1</sup>H and <sup>13</sup>C NMR chemical shift computations of 2- amino-2`(diphenylamino)-Propane-1,3-diol from 2-amino-2`bromo-1,3-propane diol are made in CDCl<sub>3</sub> [scrf= (solvent=chloroform)] by utilizing B3LYP/6-31G (d,p) basis set. The computational and experimental <sup>1</sup>H and <sup>13</sup>C NMR chemical shift of the compound computed by DFT technique are displayed in table 3.

**Polarizability calculation:** The computed values of the dipole moment ( $\mu$ ), the polarizability ( $\alpha_o$ ) and first hyperloarizability ( $\beta_{tot}$ ) by limited field approach are given in table 4 along with the corresponding components. 2-amino-2`(diphenylamino)-propane-1,3-diol from 2-amino-2`bromo-1,3-propane 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.

**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 assess 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) values, greater is the stabilization energy. Larger are the E(2) values, greater is the stability of the molecule. The lone pair of electrons present in the oxygen atom N8 is delocalized to C1 – N11 and furthermore C27 is delocalized to C1-N11, C28-C30 and C29-C32 antibonding orbitals.

Table 2				
Significant Vibrational wavenumbers obtained for2- amino-2`(diphenylamino)-Propane-1,3-diol from 2-amino-				
2`bromo-1,3-propane diol at B3LYP/6-31G(d,p) level of calculations.				

Mode No.	Theoretical frequencies (cm <sup>-1</sup> )       DFT/BL3LYP/6-31G(d,p)       Unscaled     Scaled       frequencies     frequency       scaling factor		Observed frequencies (cm <sup>-1</sup> )	Vibrational assignments PED≥10%
		= 0.9614		
1	3783	3636.98		v <sub>O14H15</sub> (96%)
2	3782	3636.01	3421	v <sub>O12H13</sub> (96%)
9	3205	3081.29		$\upsilon_{C32H36}(10\%) + \upsilon_{C34H37}(70\%)$
				$\upsilon_{C17H20}(29\%) + \upsilon_{C19H24}(25\%) + \upsilon_{C21H25}(23\%) +$
10	3195	3071.67		υ <sub>C23H26</sub> (17%)
15	3146	3024.56	2926.62	υ <sub>C5H7</sub> (96%)
16	3112	2991.88	and	υ <sub>C2H3</sub> (92%)
17	3021	2904.39	2855.66	$v_{C2H4}(49\%) + v_{C5H6}(47\%)$
18	3016	2899.58		$v_{C2H4}(43\%) + v_{C5H6}(49\%)$

v –stretching vibration;  $\beta$  – bending vibration;  $\tau$  – torsion bending.

11 allu	C Wirk Chemical Sint computed by BSL1170-51G(u,p) GIAO DF1 method				
Protons	Chemical	Observed	Carbon	Chemical	<b>Observed Chemical</b>
	shifts	chemical		shifts	shifts
		shifts			
H22	8.8		C27	156.1	
H25	7.9		C16	153.1	
H31	7.8		C18	142.5	
H24	7.8		C17	138.3	
H26	7.8	7.31-8.31	C19	134.6	
H35	7.6		C21	134.2	
H36	7.5		C32	133.6	126-139
H20	7.4		C30	132.5	
H37	7.3		C23	132.5	
H33	7.2		C29	132.2	
H7	3.8		C28	130.6	
H4	3.5		C34	125.5	
H3	3.4	3.17	C1	85.1	
H6	3.3		C5	70.3	58.83 (Aromatic C)
H9	2.5		C2	67.8	
H10	0.8	5.08			
H15	1.7				
H13	2.2	1.6			

 Table 3

 <sup>1</sup>H and <sup>13</sup>C NMR Chemical Shift computed by B3LYP/6-31G(d,p) GIAO DFT method

### Table 4

The electric dipole moment  $\mu$  (D), the mean polarizability  $\langle \alpha \rangle$  (x 10<sup>-24</sup> esu) and the First hyperpolarizability  $\beta_{tot}$  (x10<sup>-33</sup> esu) of 2- amino-2`(diphenylamino)-Propane-1,3-diol from 2-amino-2`bromo-1,3-propane diol by DFT method

Parameter	Value	Parameter	Value
$\mu_{\mathrm{x}}$	-0.144	$\beta_{xxx}$	68.19
$\mu_{y}$	-0.273	$\beta_{xxy}$	-322.02
μz	0.064	$\beta_{xyy}$	65.51
μ	0.993	$B_{yyy}$	66.75
α <sub>xx</sub>	223.91	$\beta_{xxz}$	-0.54
$\alpha_{xy}$	3.149	$\beta_{xyz}$	47.54
$\alpha_{yy}$	173.22	$\mathbf{B}_{\mathbf{y}\mathbf{y}\mathbf{z}}$	0.531
$\alpha_{xz}$	5.760	$\beta_{xzz}$	-31.41
$\alpha_{yz}$	8.991	B <sub>yzz</sub>	8.76
α <sub>zz</sub>	154.94	β <sub>zzz</sub>	25.70
α	184.03	β <sub>tot</sub>	268.12
$\alpha$ : 1a.u = 0.1482*1	0 <sup>-24</sup> esu		

 $\beta$ : 1a.u = 8.6393\*10<sup>-33</sup> esu



Fig. 2: MEP surface of2- amino-2`(diphenylamino)-Propane-1,3-diol from 2-amino-2`bromo-1,3-propane diol.

from 2-amino-2 bromo-1,5-propane dioi.						
Donor NBO	Occupancy	Acceptor NBO	Occupancy	E(2) in kcal/mol		
		BD*				
(BD) C18-C21	1.8	C16-C17	0.19	20.12		
(BD) C18-C21	1.8	C19-C23	0.17	20.27		
(BD) C19-C23	1.8	C16-C17	0.19	20.98		
(BD) C19-C23	1.8	C18-C21	0.17	20.15		
(BD) C28-C30	1.8	N11-C27	0.03	4.18		
(LP) N8	1.9	C1-N11	0.08	11.37		
(LP) N11	1.8	C16-C17	0.19	5.54		
(LP) N11	1.8	C16-C18	0.03	7.34		
(LP) O12	1.96	C1-C5	0.05	7.19		
(LP) O14	1.96	C1-C2	0.05	6.0		
(LP) C27	1.007	C1-N11	0.08	4.12		
(LP) C27	1.007	C28-C30	0.18	59.85		
(LP) C27	1 007	C29-C32	0.18	59.04		

# Table 5 Second order perturbation theory analysis of matrix in NBO basis for 2- amino-2`(diphenylamino)-Propane-1,3-diol from 2-amino-2`bromo-1 3-propane diol.



Fig. 3: HOMO image of 2- amino-2`(diphenylamino)-Propane-1,3-diol from 2-amino-2`bromo-1,3-propane diol.



Fig. 4: LUMO image of 2- amino-2`(diphenylamino)-Propane-1,3-diol from 2-amino-2`bromo-1,3-propane diol.

**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 due 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 -4.298e-2(red) to +4.298e-2(blue) units.

**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 -1.40eV, -0.015eV and 4.032eV respectively. The p<sub>z</sub> orbitals of all C, O, N atoms in the molecule participate in the HOMO orbital of the molecule. Mostly, the p<sub>z</sub> orbitals of all C moiety participate in the LUMO formation. The p<sub>z</sub> orbitals of C5 and O12 participate in the LOMO formation in a very minute level.

# Conclusion

In the present research work, a new bronopol derivative was synthesized. DFT study was performed and the structural information obtained was compared with the experimental results. They were found to be in good agreement. MEP, HOMO-LUMO, polarizability and NBO analysis for this compound.

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