



## Aromaticity, Geometry and Charge Distribution of the N,N-Dimethylantranilic Acid Conformers in Gas Phase

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This computational organic chemistry study was performed using the hybrid functional B3LYP and the MP2 method. The study demonstrates that stabilizing conformer (I) by intramolecular hydrogen bonding causes distinguished electronic structure differences with respect to (II) and (III). To our best of knowledge and to the first time in the literature, the natural population analysis atomic charges allowed to estimate the amount of the delocalized charge and provided with evidence that the hydrogen bond in (I) can alter the  $\sigma$  bond polarization. Therefore, characteristics of this model amino acid are new addition to the hydrogen bond theory.

**Key Words:** N,N-Dimethylantranilic acid, DFT, HOMA, NICS(0), NBO.

### INTRODUCTION

National Institute of Standards and Technology (NIST)<sup>1</sup> presents on the website the gas phase infrared spectrum of N,N-dimethylantranilic acid (2-(N,N-dimethylamino)benzoic acid). It shows a strong signal at nearly  $1780\text{ cm}^{-1}$  (C=O stretching) and broad weak signal (H1-O1 stretching) which represents solid evidence that gas phase structure of this compound is the neutral form (I) (Fig. 1). In addition to this structure, there are other two conformers for this amino acid in which there is no hydrogen bond between H1 and the nitrogen. Other than this experimental study, there is no theoretical study on the electronic structure aspects. Therefore, the purpose of this study is to investigate the electronic structure discrepancies among the three conformers. Unexpected variations have been disclosed which will be presented and discussed.

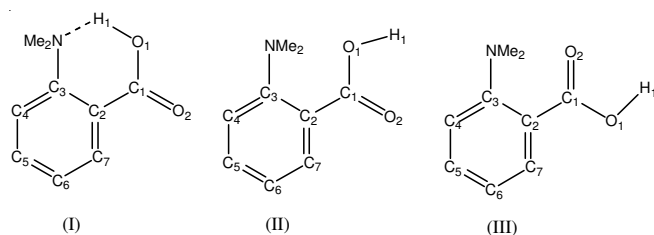


Fig. 1. Structures and the numbering system of the three conformers

### EXPERIMENTAL

All the calculations were performed using the Gaussian 03 suit of programs<sup>2</sup>. The geometries were optimized using

the B3LYP/6-31G(d) method and the B3LYP/6-311+G(2d,p) and MP2/6-311+G(2d,p) methods were used as single point energy calculations. The calculated frequencies are positive values which confirm that all the structure are true minima. The harmonic oscillator measure of aromaticity (HOMA) was calculated as described by Krygowski<sup>3</sup>. When its value is equal to 1 it means that the  $\pi$ -system is overlapping ideally, but when the value is equal to zero it means that the  $p$ -orbitals are not overlapping and the double bonds (and may be a conjugated lone pair) are fully localized. The second order perturbation (SOP) analysis and the natural population analysis (NPA) were executed using the standard NBO method<sup>4</sup>.

### RESULTS AND DISCUSSION

#### HOMA, NICS(0) and selected geometrical parameters:

Table-1 presents the harmonic oscillator measure of aromaticity (HOMA) values for the phenyl group, the N-C3-C2-C1-O2 segment and the O1-C1-O2 group, the NICS(0) from the B3LYP/6-31G(d) and the B3LYP/6-311+G(2d,p) calculations for the phenyl ring and selected geometrical parameters (entries 4, 5, 6 and 7). The data presented in entry 1 (HOMA and NICS(0)) indicate that the aromaticity does change from one conformer to another and the trend is (I) > (II) > (III).

On the other hand, The HOMA values indicate that the overlap in the N-C3-C2-C1-O2 segment increases going from (I) to (II) to (III) (III>II>I). The calculated value for conformer (I) indicates that there is a negative overlap or, in other words, an elongation in the  $\sigma$ -bonds of this segment. It is obvious

TABLE-1  
 HOMA, NICS(0) AND SELECTED GEOMETRICAL PARAMETERS

Entry	Property	Segment	Conformer (I)	Conformer (II)	Conformer (III)
1	NICS(0)	Phenyl*	10.124	8.939	8.869
	NICS(0)	Phenyl**	8.383	7.188	7.067
	HOMA	Phenyl	0.963	0.896	0.870
2	HOMA	N-C3-C2-C1-O2	-0.580	0.092	0.169
3	HOMA	O1-C1-O2	0.387	0.116	0.039
4	Bond Length	N-C3 (Å)	1.457	1.394	1.385
5	Dihedral angle	Me1-N-C3-C4	64.8	130.4	137.7
6	Dihedral angle	Me2-N-C3-C4	64.2	18.5	19.1
7	Dihedral angle	O1-C1-C2-C3	0.0	21.7	15.8 (O2)

\*B3LYP/6-31G(d); \*\*BB3LYP/6-311+G(2d,p)

 TABLE-2  
 SELECTED CHARGE DELOCALIZATION ENERGIES (kcal/mol)

Entry	Conformer	Interaction	6-31G(d)*	6-311+G(2d,p)**	6-311+G(2d,p)***
1	(I)	N→H1-O1	31.85	25.66	32.09
2		N→C2-C3	2.80	2.88	3.59
3		N→C3-C4	6.81	6.96	9.16
4		O1→C1=O2	54.11	53.05	71.54
5		C2-C3→C1=O2	16.45	16.49	21.10
6	(II)	N→H1-O1	0	0	0
7		N→C2-C3	27.80	27.78	38.84
8		N→C3-C4	3.42	3.21	4.44
9		O1→C1=O2	45.29	44.20	59.27
10		C2-C3→C1=O2	20.38	20.36	27.66
11	(III)	N→H1-O1	0	0	0
12		N→C2-C3	34.76	34.79	50.23
13		N→C3-C4	2.81	2.65	3.72
14		O1→C1=O2	41.96	41.12	55.40
15		C2-C3→C1=O2	23.27	23.37	32.98

\*B3LYP/6-31G(d); \*\*B3LYP/6-311+G(2d,p)// B3LYP/6-31G(d); \*\*\*MP2/6-311+G(2d,p)// B3LYP/6-31G(d).

that the nitrogen lone pair is involved in H-bond with H1-O1, which makes participation of the nitrogen lone pair with the rest of the segment very small. Another factor is the steric hindrance from the two methyl groups that can cause elongation in the N-C3 bond in (I) with respect to (II) and (III) (Table-1, entry 4). And, it is noted that the trend in the HOMA values of the phenyl ring is opposite to that of the N-C3-C2-C1-O2 segment. On the other hand and compared to the N-C3-C2-C1-O2 segment, the O1-C1-O2 segments includes better overlap, however, it decreases in the order (III) > (II) > (I). This suggests that these changes are related to the changes in the N-C3-C2-C1-O2 segment. The observed change is acceptable because by increasing the donation from nitrogen to O2 there should be a decrease in the donation from O1 to O2.

In conformer (I), the structure appears pretty symmetric, which results from the strong N...H1-O1 hydrogen bond. After loosing the hydrogen bond, the changes in the dihedral angles (entries 5 and 6) suggest that, in the two conformers (II) and (III), the nitrogen atom becomes involved in N → phenyl charge delocalization under the effect of the carboxylic acid group as an electron withdrawing group. This conclusion will be supported later by the second order perturbation analysis. In addition to that, the carboxylic acid group deviates from the co-planarity with the phenyl ring (entry 7) after absence of the H-bond (in II and III). The dihedral angle (entry 7) of (II) is larger than that of (III) which indicates that the steric hindrance between the nitrogen-methyl and the COOH group in (II) is larger than in (III).

Another interesting geometrical feature is the short distance separating nitrogen from H1 in conformer (I) (1.692 Å). Korth and coworkers<sup>5</sup> studied hydrogen bond systems featuring five-, six- and seven-membered pseudo-rings derived from *o*-substituted phenol. They found that the strength of the hydrogen bond increases by the increase in the size of the pseudo-ring and by the decrease in the proton-acceptor distance (2.25, 1.87 and 1.75 Å for the series of five-, six- and seven-membered rings, respectively), which allowed classifying the hydrogen bond in the seven-membered rings and therefore in conformer (I) as strong neutral hydrogen bond.

**Second order perturbation (SOP) analysis:** This analysis provides with important evidence that the hydrogen bond in conformer (I) is not a pure electrostatic interaction<sup>6</sup> but has covalent character and includes electron density delocalization<sup>7-9</sup> as illustrated in entry 1 (Table-2).

As explained by the geometry analysis and in order to support existence of an overlap in the N-C3-C2-C1-O2 segment there should be evidence on a charge delocalization in the N-C3-C2 and the C3-C2-C1-O2 units. Careful inspection of the output files confirmed these interactions and the data from the three methods are presented in the entries 2 and 5 (I), 7 and 10 (II) and 12 and 15 (III). Despite the negative HOMA value of conformer (I) (HOMA = -0.580, Table-1, entry 2), the SOP calculations indicate that there is a small charge delocalization from nitrogen to C3-C2 and even larger delocalization from C3-C2 to C1=O. The two interactions become more significant in (II) and (III). The SOP energy of N→C2-

C3 (Fig. 2) and that of C2-C3→C1=O2 (Fig. 3) were plotted against the HOMA values of the N-C3-C2-C1-O2 segment. Both figures provide evidence that the increase in the charge delocalization is accompanied by the increase in the HOMA value of the N-C3-C2-C1-O2 segment (Figs. 2 and 3) and therefore it became clear that the geometric and the charge delocalization changes are related. To our best of knowledge, the HOMA values of this segment are the lowest in the chemical literature for a segment that includes charge delocalization, which makes the three conformers unique structures.

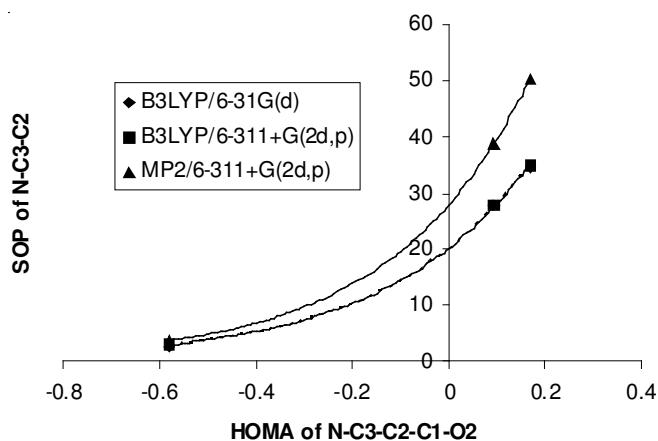


Fig. 2. Graph presenting the relation between SOP of N-C3-C2 and HOMA of N-C3-C2-C1-O2. The B3LYP/6-31G(d) and the B3LYP/6-311+G(2d,p) results are overlapping

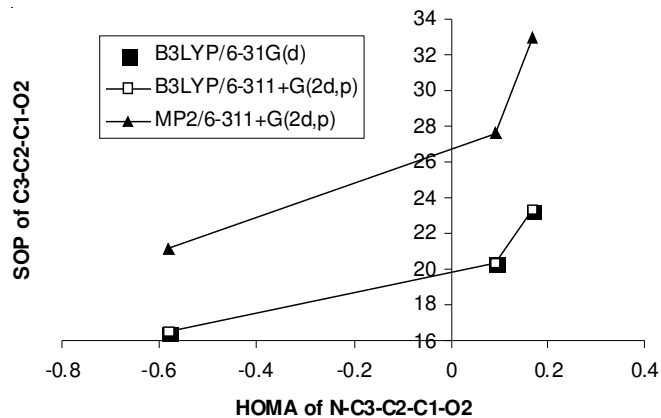


Fig. 3. Graph presenting the relation between SOP of C3-C2-C1-O2 and HOMA of N-C3-C2-C1-O2. The B3LYP/6-31G(d) and the B3LYP/6-311+G(2d,p) results are overlapping

Similarly, the observed trend in the overlap of the O1-C1-O2 segment (HOMA) is consistent with the trend of the charge delocalization energies (entries 4, 9 and 14). The trend supports that conformer (III) includes better overlap in the N-C3-C2-C1-O2 segment with respect to the other two. In addition to that, the charge delocalization energy in the O1-C1-O2 group is more significant (higher values) despite the smaller HOMA values (Table-2, entries 4, 9 and 14). This can be explained by comparing Fig. 4 (O1-C1-O2) with both Figs. 2 and 3. They clearly demonstrate that the short range overlap (O1-C1-O2; three atoms) is more efficient than the long range-two step overlap of the N-C3-C2-C1-O2 segment.

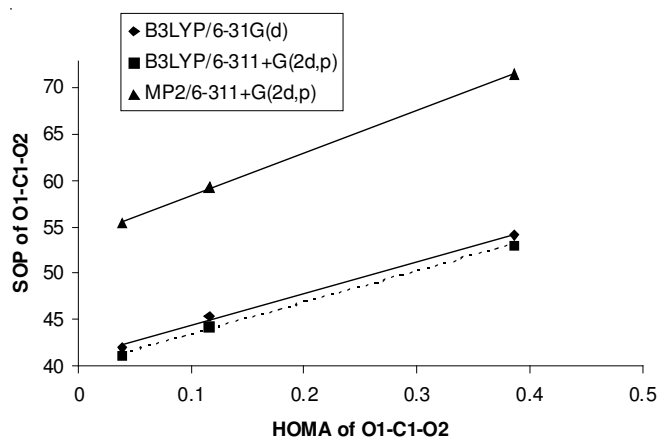


Fig. 4. Graph presenting the relation between HOMA and SOP of O1-C1-O2

The group charge changes (Table-3) are consistent with the charge delocalization energies and the structural changes (the dihedral angles, Table-1) among the three isomers. Qualitatively, the three computational methods are in agreement on the observed charge changes  $\Delta C$ . The dimethylamino group donates electron density and the trend of the donated charge amount is III > II > I. On the other hand, the phenyl and the carboxylate groups accept the charge and their negative charge increase (or the positive charge decrease) with the same trend (III > II > I). The two trends are explained based on presence of N...H1-O1 hydrogen bond in conformer (I), it localizes the nitrogen lone pair and decreases its donation to the  $\pi$ -system with respect to the conformers (II) and (III).

**Delocalized charge (N→H1-O1) in (I):** Analyzing the individual charges of the nitrogen atom and the two methyl groups (summed charges) in the 0° and the 180° rotamers

TABLE-3  
GROUPS CHARGES AND THE DIFFERENCES WITH RESPECT CONFORMER (I)

Method	Group	(I)	(II)	$\Delta C(I-II)$	(III)	$\Delta C(I-III)$
6-31G(d)*	NMe2	-0.109	-0.031	-0.078	0.034	-0.143
	COOH	0.009	-0.019	0.028	-0.032	0.041
	Phenyl	0.100	0.050	0.050	-0.002	0.102
6-311+G(2d,p)**	NMe2	-0.131	-0.048	-0.083	-0.016	-0.115
	COOH	-0.005	-0.033	0.028	-0.048	0.043
	Phenyl	0.136	0.081	0.055	0.064	0.072
6-311+G(2d,p)***	NMe2	-0.153	-0.107	-0.046	-0.083	-0.070
	COOH	0.009	-0.011	0.020	-0.022	0.031
	Phenyl	0.144	0.118	0.026	0.105	0.039

\*B3LYP/6-31G(d); \*\*B3LYP/6-311+G(2d,p)// B3LYP/6-31G(d); \*\*\*MP2/6-311+G(2d,p)// B3LYP/6-31G(d).

(Table-4) illustrates that the charge of nitrogen decreased and the charge of the two methyl groups increased. To our best of knowledge, this is the first evidence in the chemical literature on the ability of a hydrogen bond to affect a  $\sigma$ -bond polarization.

TABLE-4  
NPA CHARGES OF NITROGEN AND THE  
TWO METHYL GROUPS OF CONFORMER (I)

Group	Angle <sup>a</sup> (°)	6-31G(d) <sup>b</sup>	6-311+G(2d,p) <sup>c</sup>	6-311+G(2d,p) <sup>d</sup>
N	0	-0.547	-0.601	-0.657
	180	-0.507	-0.567	-0.619
2Me	0	0.438	0.470	0.504
	180	0.372	0.414	0.453
NMe <sub>2</sub>	0	-0.109	-0.131	-0.153
	180	-0.135	-0.153	-0.166

<sup>a</sup>Dihedral angle H1-O1-C1-C2; <sup>b</sup>B3LYP/6-31G(d); <sup>c</sup>B3LYP/6-311+G(2d,p)//B3LYP/6-31G(d); <sup>d</sup>MP2/6-311+G(2d,p)//B3LYP/6-31G(d)

The delocalized charge from Me<sub>2</sub>N to H1-O1 can be calculated simply by finding the charge difference of Me<sub>2</sub>N in the two rotamers of conformer (I) (at 0° and 180°, Table-4). The values were calculated using the B3LYP/6-31G(d), B3LYP/6-311+G(2d,p) and MP2/6-311+G(2d,p) and they are equal to 0.026, 0.022 and 0.013 of the electron charge (2.6, 2.2 and 1.3 %), respectively. These per cents are small but consistent with the fact that a hydrogen bond is only of similar per cent (*ca.* 1%) compared to a covalent bond.

### Conclusion

The calculations based on the B3LYP/6-31G(d), B3LYP/6-311+G(2d,p) and MP2/6-311+G(2d,p) produced homogeneous and well-connected sets of data. The results can be summarized in the following points: (1) The calculations demonstrate that breaking the hydrogen bond in (I) to form (II) and (III) can cause significant changes in the phenyl group aromaticity, the geometries and the charge distribution.

(2) Among the three conformers, the changes in the geometries affect the charge delocalization directly as confirmed by the SOP-HOMA diagrams. (3) Despite existence of charge delocalization in the N-C3-C2-C1-O2 segment, the steric hindrance caused very low geometric overlapping including negative HOMA value (in (I)), which are the first cases of its type. (4) To our best of knowledge and to the first time in the literature it is possible to observe and estimate the delocalized charge amount in a H-bond which has been achieved based on the natural population analysis scheme. (5) To our best of knowledge and to the first time in the literature, a close look at the nitrogen and the methyl group charges indicates that the hydrogen bond can alter the atomic charge distribution in a sigma bond and therefore its polarization.

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