

## 1-알콕시-4-니트로아닐린들의 糖度에 관한 研究

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(1973. 1. 22 접수)

## Sweet Taste Mechanism of 1-Alkoxy-4-nitroaniline

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(Received Jan. 22, 1973)

**요 약.** 반실험적인 양자역학 이론인 extended Hückel theory를 nitroaniline, 1-methoxy-4-nitroaniline 과 1-ethoxy-4-nitroaniline 에 적용하여 정량적으로 변화하는 sweetness 기구를 구명코저 nitroaniline 을 coplanar 로 두고 ortho 치환체의 geometrical rotation 을 시켰을 때 charge density 와 sweetness 와의 상관 관계를 설명하였다.

**Abstract.** A semiempirical molecular orbital theory which is known as extended Hückel theory is applied to explain the sweet taste mechanism of nitroaniline, 1-methoxy-4-nitroaniline, and 1-ethoxy-4-nitroaniline which has different sweetness respectively.

In this paper, the assumption is made that the nitroaniline is coplanar. The relationship between charge density and sweetness has been calculated according to the geometrical rotation of the orthosubstitute of nitroanilines.

It has been shown that the calculated results are consistent with the experimental order of the relative sweetness.

### Introduction

Many sweet compounds have been known in the past. But it is only in recent years that an extensive investigation of the subject has been undertaken. Ferguson and his co-workers examined<sup>1-5</sup> the physiological aspect of the taste and attempted to correlated sweetness with certain physical properties.

It has been observed<sup>6,7</sup> that many 1-substituted 4-nitroanilines in the Fig. 1 are intensely

sweet, where as the isomeric 1-substituted 6-nitroanilines (II) in the Fig. 1 are bitter or tasteless.

This striking difference in taste of isomeric compound has aroused our interest in their

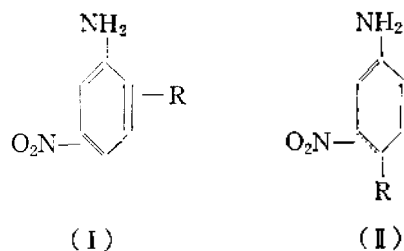


Fig. 1.

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Table 1. Relative sweetness (sucrose=1)

R	I <sup>7,8</sup>	II <sup>9</sup>
-H	40	—
-OCH <sub>3</sub>	167	tasteless
-CH <sub>3</sub>	290	tasteless
-Br	715	tasteless
-OCH <sub>2</sub> CH <sub>3</sub>	950 <sup>8</sup>	—
-OCH <sub>2</sub> CH <sub>2</sub> CH <sub>3</sub>	4,000 <sup>8</sup>	—

physiological properties. In spite of the attempts of many chemists, no reliable, widely applicable correlation has been found between the rationalistic chemical basis of the taste sense and molecular properties of substances. It appears that chemoreception depends upon several properties.

Attention has been given to the electron distributions in these substituted nitroanilines which arises from configurational difference in the molecules which is due to steric compression. We have calculated charge density by the extended Hückel theory. Good relationship between the sweetness and the charge density of the substituted nitroanilines were found.

### Calculation

In the extended Hückel theory developed by Hoffmann<sup>9</sup>, the expansion of a molecular orbital as a linear combination of the Slater type atomic orbitals yields

$$\psi_i = \sum_{j=1}^n c_{ij} \phi_j \quad (1)$$

which is given as,

$$\phi_j = N_r r^{n-1} \exp(-rz) Y_{l,m}(\theta, \phi) \quad (2)$$

where  $Z$  is the orbital exponent for the AO's and other terms have their usual significances<sup>10</sup>. The summation in Eq. (1) is over all valence orbitals used in constructing the molecular orbital, namely the  $1_s$  is orbital for hydrogen,

$2p_x, 2p_y, 2p_z$ , and  $2p_x$  orbitals for the second row elements.

In solving the usual secular equation (3), the Coulomb integrals  $H_{ii}$  are chosen as the negative of valence state ionization potential (VSIP) and

$$\sum_{i=1}^n (H_{ij} - ES_{ij}) C_{ij} = 0 \quad J=1, 2, \dots, n \quad (3)$$

where  $H$ , is the Hamiltonian operator,  $E$ , the energy,  $S$ , the overlap integral, and  $C$ , the orbital coefficient. All overlap integrals are considered. For estimating the off-diagonal matrix elements  $H_{ij}$ , the Wolfsberg-Helmholtz approximation<sup>11</sup> is used. The value of  $K$  has been chosen as 1.75 in accordance with earlier works.<sup>8,13,14</sup> The computer input data consisted of the orbital exponents  $Z$ , valence state ionization potential and accurate coordinates of atoms. The  $Z$  and VSIP values are summarized in Table 2.

$$H_{ij} = 0.5K(H_{ii} + H_{jj})S_{ij} \quad (4)$$

It is therefore necessary to determine the three dimensional coordinates of each atom in the conformation selected for calculation. These are derived using a vector programme which locates each atom in space in Cartesian coordinates.

The bond lengths used were C-C=1.54, C-N=1.47, C-O=1.42, N-O=1.21, C-H=1.09, C=C=1.40, C-N=1.36, N-H=1.02 all in angstroms. All bond angles were  $\angle CNO = 118^\circ$ ,  $\angle CCC = 120^\circ$ ,  $\angle CNH = 106.6^\circ$ ,  $\angle COC = 119^\circ$ , and alkyl parts may be considered tetrahedral.

### Results and Discussion

If bulkiness of ortho substituted group of the nitroanilines is increased, one might expect that i) the base strengths will be increased and ii) the positive charge of nitrogen atom in nitro group will be increased.

Examination of data of Table 3 reveals that these expectations are true.

This difference in strength arises from configurational difference in the molecules. These facts are shown with the help of Fig. 2.

Table 2. Coulomb integrals<sup>12</sup>

Electron	Value(eV)
N 2 <sub>p</sub>	-26.00
N 2 <sub>p</sub>	-13.40
O 2 <sub>p</sub>	-35.30
O 2 <sub>p</sub>	-17.76
C 2 <sub>p</sub>	-21.40
C 2 <sub>p</sub>	-11.40

Slater exponent

Atom	Value
H	1.00
O	1.625
N	1.925
O	2.275

Table 3.  $pK_a$  values for some substituted anilines<sup>4</sup>

Substituent	$pK_a$ of aniline	$pK_a$ of 5-nitroaniline
H	4.58	2.54
2-CH <sub>3</sub> O	4.49	2.49
2-CH <sub>3</sub>	4.38	2.30
2-Br	2.60	0.52
4-CH <sub>3</sub> O	5.26	3.36
4-CH <sub>3</sub>	5.05	2.86
4-Br	3.91	1.80

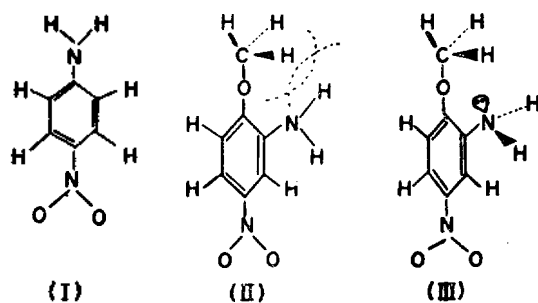


Fig. 2.

The configuration needed for maximum interaction of  $\pi$ -electrons of benzen ring with the unshared electrons of nitrogen is that in which all atoms of the molecule are in no steric compression for nitro-aniline, because there is enough space to accomodate both the volumes occupied by the hydrogen attached to the nitrogen of the amino group and by the ortho hydrogen atom. In 1-methoxy-4-nitroaniline, a planar configuration compresses the ortho methoxy and one of the hydrogen attached to the nitrogen, as indicated in structure II of Fig. 2. To avoid this strain, the amino group and alkoxy group are twisted from the plane of the benzene ring as it be seen in the structure(III) of Fig. 2.

As a result, the electron pair of nitrogen is more localized and the basicity of the 1-methoxy-4-nitroaniline becomes greater than that of nitroaniline. To evaluate a steric hindrance

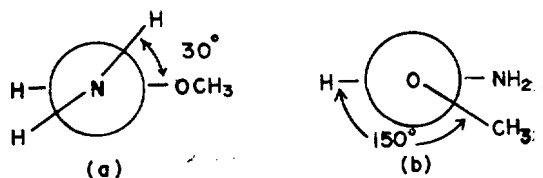


Fig. 3. Calculated conformation of 2-methoxy-4-nitroaniline

a) Amino group and benzene ring relationship.

b) Methyl group and benzene ring relationship.

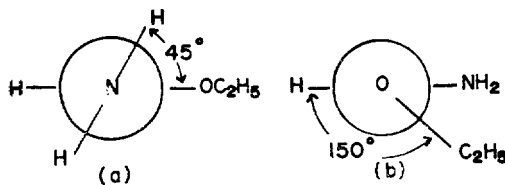


Fig. 4. Calculated conformation of 2-ethoxy-4-nitroaniline.

a) Amino group and benzene ring relationship.

b) Ethyl group and benzene ring relationship.

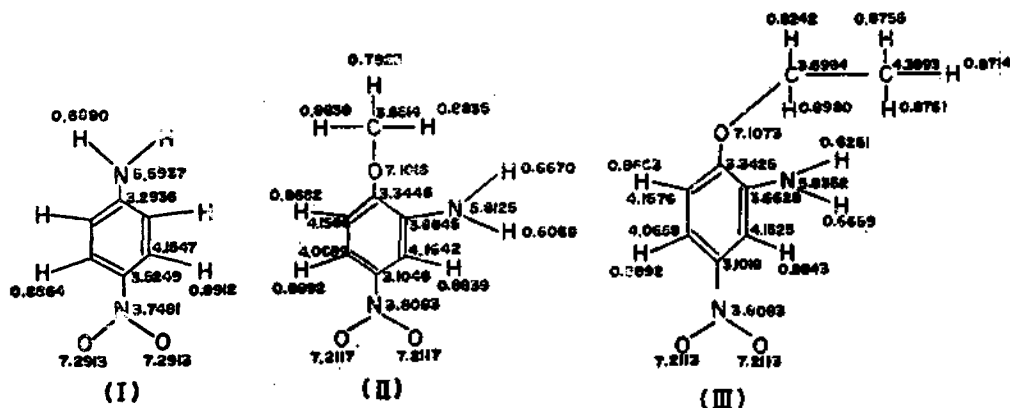


Fig. 5.

effect on the charge density of amino group, we calculated the charge density of nitroaniline, 1-methoxy-4-nitroaniline and 1-ethoxy-4-nitroaniline.

In this calculation, the following assumption is made; nitro-aniline is coplanar, amino group and methoxy group of 1-methoxy-4-nitroaniline are twisted  $30^\circ$  and  $150^\circ$ , respectively from the benzene ring as shown in Fig. 3, and amino group and ethoxy group of 1-ethoxy-4-nitroaniline are twisted  $45^\circ$  and  $150^\circ$  respectively from the benzene ring as shown in Fig. 4.

The calculated results shown that negative charge density on nitrogen atom of amino groups and positive charge density on nitrogen atom of nitro group are increased as shown in Fig. 5.

These values on the nitrogen satisfy the order of the relative sweetness of the substituted nitroanilines and separated charge on the nitrogen control to bind with an acceptor molecule as a complex.

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