Chapter IV

Electron Density and Odor
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ELECTRON DENSITY AND ODOR

One of the important factors influencing odor quality as well as intensity is the electron density distribution over atoms in an odorous molecule. The greater the electron density, the greater should be the intensity of odor. This is illustrated by the highly intense odors of allyl isothiocyanate ($\text{CH}_2 = \text{CH} - \text{CH}_2 - \text{N} = \text{C} = \text{S}$), sec.-butyl mustard oil ($\text{CH}_2\text{N}_\text{H}_2$), phenyl isothiocarbimide ($\text{CH} - \text{N} = \text{C} = \text{S}$), chlorobenzene, benzene, toluene, and mesitylene ($\text{CH}_3\text{C}_6\text{H}_4\text{CH}_3$). The last substance has insupportibility of 43 mg/m$^3$.

Other indirect support is obtained from adsorption of odorous molecules on silica gel. The -OH groups of silica gel are bound by covalent links to silicon atoms. When adsorption of molecules like chlorobenzene ($\text{C}_6\text{H}_5\text{Cl}$), benzene ($\text{C}_6\text{H}_6$), toluene ($\text{C}_6\text{H}_5\text{CH}_3$), and mesitylene ($\text{C}_9\text{H}_{12}$) takes place, it is found that there is a considerable shift of the frequency of the surface -OH groups. The amount of the shift is increasing in sequence.

Chlorobenzene, benzene, toluene, mesitylene.
i.e. in the direction of increasing $\pi$-electron density in
the ring, and consequently with increasing electron donating
properties.

It is also reported that benzene forms $\pi$-complexes
such as $(\text{C}_6\text{H}_6)_2\text{M}$ in which $\text{M}$ is $\text{Cr}$, $\text{Mo}$, $\text{W}$ and $\text{V}$, and it
looses aromatic character. Adsorption of benzene on nickle
and copper support the fact that $\pi$-electron character has
a major role in the process of adsorption. Therefore, a
decrease or loss of $\pi$-electron density is quite evident in
$\pi$-complexes and adsorption processes. It may be the same
reason, why metallic containers are no good for storage of
fragrant materials, because metal-$p$ interaction will be
quite prominent.

In benzene itself, all the carbon atoms are
equivalent, but, as has been known, the presence of substituents
or of hetero atoms, profoundly affects the distribution of
$\pi$-electrons. Certain groups have an electron releasing
effect and increase the $\pi$-electron density all around the
aromatic ring and especially at the ortho-para positions
(as in fig. 1) other groups have two opposing effects and
increase the $\pi$-electron density at the ortho-para positions,
but reduce it at the meta positions. Nitro, carbonyl and
carbethoxy, and certain other groups, on the other hand, have
an electron attracting effect and decrease the charge on the
aromatic ring, especially at the ortho-para positions (as in
fig. 2). Under these circumstances, the meta positions have a greater $\pi$-electron density than the ortho-para positions. The Halogens also seem, in general, to have a resultant electron attracting effect, but they are exceptional in that they appear to leave the ortho-para positions more charged than the meta positions:

\[
\begin{align*}
\text{(1)} & \quad x & & -d & & +d \\
\text{(2)} & \quad y & & -d & & +d 
\end{align*}
\]

This fact is of very considerable value in the study of aromatic substituted compounds.

Hammett's substituent constants:

<table>
<thead>
<tr>
<th>Substituent</th>
<th>Hammett's Constant $\sigma$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$p$-NH$_2$</td>
<td>-0.660</td>
</tr>
<tr>
<td>$p$-Cl</td>
<td>-0.0269</td>
</tr>
<tr>
<td>$p$-C$_2$H$_5$</td>
<td>-0.25</td>
</tr>
<tr>
<td>$m$-Me$_2$N</td>
<td>-0.211</td>
</tr>
<tr>
<td>$p$-Me$_2$N</td>
<td>-0.205</td>
</tr>
<tr>
<td>$p$-t-C$_4$H$_9$</td>
<td>-0.197</td>
</tr>
<tr>
<td>$p$-Cl</td>
<td>-0.170</td>
</tr>
<tr>
<td>$m$-NH$_2$</td>
<td>-0.161</td>
</tr>
<tr>
<td>$p$-C$_6$H$_5$</td>
<td>+0.009</td>
</tr>
<tr>
<td>$m$-Cl</td>
<td>+0.062</td>
</tr>
<tr>
<td>$m$-CH$_3$O</td>
<td>+0.115</td>
</tr>
<tr>
<td>$m$-C$_2$H$_5$</td>
<td>+0.15</td>
</tr>
<tr>
<td>$p$-C$_6$H$_5$</td>
<td>+0.213</td>
</tr>
<tr>
<td>$p$-Cl</td>
<td>+0.227</td>
</tr>
<tr>
<td>$p$-Br</td>
<td>+0.232</td>
</tr>
<tr>
<td>$p$-I</td>
<td>+0.276</td>
</tr>
<tr>
<td>Substituent</td>
<td>Value</td>
</tr>
<tr>
<td>------------</td>
<td>--------</td>
</tr>
<tr>
<td>p-C₂H₅</td>
<td>-0.151</td>
</tr>
<tr>
<td>p - C₃H₇</td>
<td>-0.151</td>
</tr>
<tr>
<td>m-CH₃</td>
<td>-0.069</td>
</tr>
<tr>
<td>p - CH₃S</td>
<td>-0.047</td>
</tr>
<tr>
<td>m-CH₃</td>
<td>-0.069</td>
</tr>
<tr>
<td>m - F</td>
<td>0.337</td>
</tr>
<tr>
<td>m - I</td>
<td>0.352</td>
</tr>
<tr>
<td>m - COOH</td>
<td>0.355</td>
</tr>
<tr>
<td>m - Cl</td>
<td>0.373</td>
</tr>
<tr>
<td>m - CHO</td>
<td>0.391</td>
</tr>
<tr>
<td>m - Br</td>
<td>0.391</td>
</tr>
<tr>
<td>m - CN</td>
<td>0.608²</td>
</tr>
<tr>
<td>p - CN</td>
<td>0.656ᵇ</td>
</tr>
<tr>
<td>m - NO₂</td>
<td>0.710</td>
</tr>
<tr>
<td>p - COOH</td>
<td>0.723</td>
</tr>
<tr>
<td>p - NO₂</td>
<td>0.773</td>
</tr>
<tr>
<td>p - Cl₃CO</td>
<td>0.874</td>
</tr>
<tr>
<td>p - CHO</td>
<td>1.126</td>
</tr>
<tr>
<td>p - NO₂</td>
<td>1.27</td>
</tr>
</tbody>
</table>

= +ve values - indicates that it attracts electron from the ring.

= -ve values - indicates that the substituent transfers charge (electronic charges) to the ring. The magnitude of is indicative of the magnitude of the charge transferred.

*a to be used for all reactions of C₆H₆ except those of aniline and phenol

*b to be used for the reactions of derivatives of aniline and phenol
-I inductive effect of the groups tend to decrease the electron density on all the annular carbon atoms, but the +\( \text{II} \) effect tends to increase it specifically at the ortho and para positions. Para alkoxyl group is conjugated with the side chain, but a meta alkoxyl group is not.

With the halogens, the -I and +\( \text{II} \) effects are also opposed. In this case the constants indicate that the halogens produce a decrease in \( \overline{\text{\text{\upshape \&}}} \) electron density all over the ring, but a smaller decrease in para position for the meta position the halogen is conjugated with the side chain.

In the case of -\( \text{CH}_2 \), -CN, -NO\(_2\) and -COOH substituents, the -I and -\( \text{II} \) effects reinforce one another when the substituent is in the para position, and for this reason the constants have greater values for the para than for the meta positions.

The effect of the common substituents

\[
\begin{array}{cccc}
\text{MeO} & -1 & +\text{II} & \text{NO}_2 & -1 & -\text{II} \\
\text{\text{\text{\(\text{\&}\)}}} & -1 & +\text{II} & \text{Cl} & -1 & -\text{II} \\
\text{F} & -1 & +\text{II} & \text{COOH} & -1 & -\text{II} \\
\text{Cl} & -1 & +\text{II} & \text{COOEt} & -1 & -\text{II} \\
\text{Br} & -1 & +\text{II} & \text{Me} & +\text{II} & +\text{II} \\
\text{I} & -1 & +\text{II} & & & \\
\end{array}
\]

\( \overline{\text{\text{\upshape \&}}} \) electron density distribution in many molecules has been carried out by an approximate valence bond method and
It has also been noted that it is possible to calculate somewhat similar $\pi$-electron density diagrams by H.O. method, and these are found to be in substantial agreement with those obtained by the valence bond approximation.\(^7\)

$\pi$-electron density diagrams of some of the molecules are given below.

- Pyridine
  - V.B. Method\(^6\)
  - M.O. Method\(^7\)

- Pyrrole
- Pyridine

- Furan\(^6\)
- Thiophene\(^6\)
- Quinoline\(^9\)
The electron density distribution diagrams support the fact that these systems should have different odors and it has been found in various text descriptions that they have different odors.

The effect of the incoming new substituent on the odor of the prevailing thiocarbamide can be seen for the mustard oil. For example, phenyl thiocarbamide is pungent but the electron attracting groups -Cl, -Br and -I attract the electrons to themselves and decrease the delocalized electron density over the phenylthiocarbamide system, thereby, decreasing the odor intensity. The odor intensity decrease for chloro, bromo and iodo compounds can be explained by using Hammett's substituent constants.
The same concept is applicable to the following system and it explains the nature of differences in odor.

dichlorophenyl thiocarbimides

2,4 dichlorophenyl thiocarbimide 甜

2,5 dichlorophenyl thiocarbimide 强烈

3,5 dichlorophenyl thiocarbimide 强烈

The same electron donating and attracting effects can explain the odor of various examples. For example, the odor of phenyl thiocarbimide is strongly pungent by itself due to five $p\overline{p}$ electrons in the system and one being highest delocalized due to $\equiv N = C = O$. This property of odor
is further increased by substitution in the meta position and m-tolylthiocarbimide is very strongly pungent, due to overall increase in the $\pi$-electron density at various points over the molecule. But when the -CH$_3$ is substituted at the para position the molecule becomes more polar due to the ortho para activating effect.

![Structural diagrams of Pherylthio-carbimide, m-tolylthiocarbimide, and p-tolylthiocarbimide](image)

Phenylthio-carbimide  m-tolylthiocarbimide  p-tolylthiocarbimide

Hammett's Constants  $-0.69$  $-0.170$

Thus it is very likely that the electronic effect of the new substituent over the basic system would change the type and intensity of the odor on the basis of redistribution of electron intensity and the degree of electronic delocalization of p $\pi$ charge clouds in present in the basic system. For example, odor of 3,5-xylene-1-ol is strongly phenolic odor but 2,6-xylene-1-ol has winter green odor.$^{14}$
The change in odor from strong phenolic odor of 3,5-xylen-1-ol to the weak odor of 2,4-xylen-1-ol can be explained on the electronic basis.

In a cyclic ring when the double bonds are close to each other in one part, the molecule has a greater π-electron density in one part as compared to the other part, producing a highly odorous molecule with a very low threshold values.15
e.g. $\beta$-ionone $I_w = 0.007$ ppb. But for the open chain ketone, e.g. pseudoionone $I_w = 50$ ppb and for geranylacetone $I_w$ is 60 ppb. It seems reasonable that in the open chain structure there is a double bond at the other end of the $C=\bigcirc$ which stretches in the opposite direction and, therefore, decreases the odor intensity.
Together with the change in threshold a small change in quality of odor which is illustrated by Pittet and Hniza on comparing with pyrazine, pyridine and thiazole derivatives with changes in substitution (substituents). Some compounds with their odor are given below:

### Flavor properties of heterocycles

**Pyrazine compounds:**

Name of the compound | Flavor properties:
---|---
A. 1. 2-methyl pyrazine | nutty, roasted
2. 2-propyl pyrazine | green vegetable
3. 2-isopropylpyrazine | green, nutty
B. 1. 2-ethoxypyrazine | sweet, nutty
2. 2-butoxy pyrazine | green vegetable

**Thiazole compounds:**

C. 1. 2-methyl thiazole | green, vegetable
2. 2-propylthiazole | green, herby, nutty
3. 2-isopropylthiazole | green, vegetable
D. 1. 2-ethoxy thiazole | sweet, nutty
2. 2-butoxy thiazole | green, vegetable

**Pyridine compounds:**

E. 1. 2-methyl pyridine | green
2. 2-propyl pyridine | sweet, green
3. 2-isopropylpyridine | green, vegetable
we entirely agree with the concept laid down by P. Saito and Igusa to the odor similarities in nitrogen heterocycles of isosteric pyridines, pyrazines and thiazoles. According to them, an important factor influencing odor quality is charge distribution. Applying the molecular orbital calculation, the following charge distribution takes place in pyridine pyrazine and thiazole molecules.\textsuperscript{17}

\begin{center}
\begin{tabular}{ccc}
\textbf{Pyridine} & \textbf{hydrazine} & \textbf{thiazole} \\
\begin{tikzpicture}
\draw[thick] (0,0) -- (1,1) -- (2,0) -- (1,-1) -- (0,0);
\node at (0.5,0.5) {+0.049};
\node at (0.5,-0.5) {-0.010};
\end{tikzpicture} & \begin{tikzpicture}
\draw[thick] (0,0) -- (1,1) -- (1,-1) -- (0,0);
\node at (0.5,0.5) {+0.041};
\node at (0.5,-0.5) {-0.052};
\end{tikzpicture} & \begin{tikzpicture}
\draw[thick] (0,0) -- (1,1) -- (1,-1) -- (1,0) -- (0,0);
\node at (0.5,0.5) {+0.034};
\node at (0.5,0.0) {-0.194};
\end{tikzpicture}
\end{tabular}
\end{center}

They consider that the carbon atoms in the 2 and 4 positions tend to be \(1\)-electron deficient and are separated by electron rich nitrogen atom; the ring nitrogens of pyrazine and pyridine exert a similar effect. However, the carbon atom of position 5 of the thiazole ring tends to be \(1\)-electron rich and is adjacent to the electron deficient S-atom (due to electron donation of two electrons to the \(1\) system). Therefore, functional groups on the C-5 of the thiazole are influenced by different
electronic distributions from those situated at C-2 and C-4 and hence, the charge distribution plays undoubtedly an important role in determining the orientation of the thiazole ring and its substituents at the nasal receptor site through the creation of a polarized odorant receptor complex. Of course, much critical information can only be obtained if odor of a large number of a series of such compounds are studied by scientists. Somehow \( \pi \)-electron density distribution is very significant in changing the quality and also the intensity. For example, odor of benzene and pyridine are quite different.

Systematic stretching of charge clouds has a prominent role in changing the odor type and intensity has been discussed in next chapter.
REFERENCES