DIRECTIVE EFFECTS IN ELECTROPHILIC SUBSTITUTION OF
SUBSTITUTED BipHENYLS AND 6 SUBSTITUTED STYRENES

by

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1963
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APPROVAL BY THESIS DIRECTOR

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Assistant Professor of Chemistry

Date
ACKNOWLEDGMENT

I express my thanks to Dr. John P. Schaefer for his direction and assistance in my graduate work but particularly for his patience with me.
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ABSTRACT

An explanation of the 2',4' directive effect in substituted biphenyls and the ortho, para directive effect of β-substituted styrenes in aromatic substitution, where the substituent is normally meta directing is given. On the basis of orientation of substitution in sterically hindered systems and rate data the orientation is concluded to be due to resonance interaction with the substituted ring in biphenyls and by analogy to interaction with the double bond in β-substituted styrenes. Isomer distributions calculated assuming resonance interaction are in agreement with experimentally found distributions for the two systems.
DISCUSSION

Relative rates and orientation of aromatic substitution are qualitatively predictable by considering the mechanism of aromatic substitution and electronic effects of ring substituents.

The mechanism for aromatic substitution involves attack on a carbon bearing a hydrogen by an electrophile, forming an intermediate or transition state. Subsequent elimination of a proton from that carbon produces the substituted aromatic.

\[
\text{Ar} \quad X^+ \quad \text{Ar}^+ \quad \text{Ar} \quad X
\]

The directive effect of substituents can usually be rationalized by drawing resonance forms for the ground state molecule. The site of attack ortho, para or meta to the substituent, however, is determined by the electronic stabilization of the transition state relative to the ground state.

To illustrate this, the transition state resulting from electrophilic attack on anisole in the ortho or para position is stabilized by four principal resonance forms.
On the other hand, if attack occurred at the meta position, only three principal resonance forms could be written.

Therefore, the para or ortho transition state should be of lower energy relative to the ground state and the products of electrophilic attack should be predominantly the ortho and para isomers. A consideration of the electronic distribution in the ground state would lead to the same conclusion on orientation.

These suppositions are supported by the fact that on acetylation or benzoylation anisole yields 66 and 88.6 per cent of the respective para isomers.

Electrophilic attack on nitrobenzene yields predominantly the meta derivative. Here the nitro group deactivates the ring inductively and selectively deactivates the para and ortho positions by means of resonance.
If again there is agreement of ground state electronic distribution and transition state stability, then the attacking electrophile would be expected to substitute in the meta position, for the meta transition state should have lowest energy. In this case, the transition state for meta attack is stabilized by three resonance forms as is the transition state for para or ortho attack. However, for para or ortho attack, one resonance form places a positive charge next to the nitrogen of the nitro group, which has a formal plus one charge, a situation energetically unfavorable. Therefore, meta substitution should occur. This is in agreement with the isomer distribution found on nitration of nitrobenzene. Nitration at 0°C. produces 6.4% ortho, 93.2% meta, and 0.3% para dinitrobenzene.

Another strongly meta directing group is the quaternary ammonium group [-N(R)₃]. Here direct resonance interactions are not possible so there is little selective deactivation in the ground state. Therefore, the directive effect must be rationalized primarily on the transition state energy. The transition state argument is the same as for nitrobenzene. In any position of attack three resonance forms
are possible; however, ortho and para attack places a positive charge on the carbon next to the positive quaternary ammonium group for one resonance form.

\[
\begin{array}{c}
\text{\ce{+\(N(CH_3)_3\)}} \\
\text{+\(N(CH_3)_3\)} \\
\text{+\(N(CH_3)_3\)} \\
\text{+\(N(CH_3)_3\)}
\end{array}
\]

This resonance for (A) being considered a small contributor to the overall resonance energy results in the ortho or para transition state being stabilized by two principal resonance forms, and therefore is less stabilized. On nitration of the trimethyl phenylammonium ion Ingold\(^6\) reports that 100% meta substitution occurs.

A consideration of the directive effects of substituted biphenyls and \(\beta\) substituted sytrenes is more complex and the experimental observations may appear anomolous if reasoning is based on the normal directing effects of a substituent.

From a survey of reactions of substituted biphenyls (Table I) undergoing electrophilic attack, two generalizations can be made regarding the position of substitution. First of all, biphenyls with strongly activating groups undergo attack and substitution in the ortho positions
### TABLE I

**MONOSUBSTITUTED BIPHENYLS REACTING TO PRODUCE DISUBSTITUTED BIPHENYLS**

![Diagram of biphenyls](image)

**A. Reactions of 4-Substituted Biphenyls**

<table>
<thead>
<tr>
<th>Substituent X</th>
<th>Reaction</th>
<th>Position of Substitution of Y</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO₂</td>
<td>Nitration</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>NO₂</td>
<td>Acetylation</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>CHO</td>
<td>Nitration</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>COOH</td>
<td>Nitration</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>H</td>
<td>Nitration</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>H</td>
<td>Sulfonation</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>CH₃</td>
<td>Nitration</td>
<td>X</td>
<td>?</td>
</tr>
<tr>
<td>NHCR</td>
<td>Nitration (highly acidic)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>NHCR</td>
<td>Chlorosulfonation</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>NHCR</td>
<td>Bromination</td>
<td>-</td>
<td>X</td>
</tr>
</tbody>
</table>
TABLE I—Continued

A. Reactions of 4-Substituted Biphenyls (continued)

<table>
<thead>
<tr>
<th>Substituent X</th>
<th>Reaction</th>
<th>Position of Substitution of Y</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHSO₂⁺NO₂</td>
<td>Nitration (Ac₂O)</td>
<td>2, 3</td>
<td>8</td>
</tr>
<tr>
<td>OCH₃</td>
<td>Bromination</td>
<td>60, 30</td>
<td>8</td>
</tr>
</tbody>
</table>

B. Reactions of 3 Substituted Biphenyls

<table>
<thead>
<tr>
<th>Substituent X</th>
<th>Reaction</th>
<th>Position of Substitution of Y</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO₂</td>
<td>Bromination</td>
<td>100%</td>
<td>34</td>
</tr>
<tr>
<td>NO₂</td>
<td>Nitration</td>
<td>X, X</td>
<td>34</td>
</tr>
<tr>
<td>CH₃</td>
<td>Nitration</td>
<td>X, X</td>
<td>31</td>
</tr>
<tr>
<td>NHCR</td>
<td>Halogenation</td>
<td>X, X</td>
<td>34</td>
</tr>
<tr>
<td>NHCR</td>
<td>Nitration</td>
<td>X, X</td>
<td>34</td>
</tr>
<tr>
<td>NHCR</td>
<td>(low acidity)</td>
<td>X, X</td>
<td>34</td>
</tr>
<tr>
<td>NHCR</td>
<td>Nitration</td>
<td>X, X</td>
<td>34</td>
</tr>
</tbody>
</table>
### TABLE I--Continued

C. Reactions of 2 Substituted Biphenyls

<table>
<thead>
<tr>
<th>Substituent X</th>
<th>Reaction</th>
<th>Position of Substitution of Y</th>
<th>3</th>
<th>4</th>
<th>2'</th>
<th>3'</th>
<th>4'</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO₂</td>
<td>Chlorosulfonation</td>
<td></td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
<td>70%</td>
<td>35</td>
</tr>
<tr>
<td>NO₂</td>
<td>Acetylation</td>
<td></td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
<td>X</td>
<td>32</td>
</tr>
<tr>
<td>NO₂</td>
<td>Nitration</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>39%</td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>Cl</td>
<td>Nitration</td>
<td></td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
<td>X</td>
<td>36</td>
</tr>
<tr>
<td>NHAc</td>
<td>Chlorosulfonation</td>
<td></td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
<td>X</td>
<td>35</td>
</tr>
<tr>
<td>NHAc</td>
<td>Nitration</td>
<td></td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
<td>78%</td>
<td>22</td>
</tr>
<tr>
<td>NHAc</td>
<td>Bromination</td>
<td></td>
<td>100%</td>
<td></td>
<td>-</td>
<td>-</td>
<td></td>
<td>22</td>
</tr>
<tr>
<td>NHSO₂(NO₂)(m)</td>
<td>Nitration</td>
<td></td>
<td>X</td>
<td></td>
<td>-</td>
<td>-</td>
<td></td>
<td>17</td>
</tr>
<tr>
<td>NHSO₂(CH₃)(p)</td>
<td>Bromination</td>
<td></td>
<td>100%</td>
<td></td>
<td>-</td>
<td>-</td>
<td></td>
<td>17</td>
</tr>
</tbody>
</table>
of the substituted ring. Secondly, biphenyls bearing a deactivating group, where deactivation results from resonance or inductive effects, substitution occurs in the unsubstituted ring in the 2' and 4' positions.\textsuperscript{7}

On bromination of 4-methoxybiphenyl a sixty per cent yield of the 3-bromo-4-methoxybiphenyl is obtained;\textsuperscript{8} this illustrates the first generalization. On the other hand, nitration of 4-nitrobiphenyl occurs in the 2' and 4' positions.\textsuperscript{9} Since the nitro group is a deactivating group, 4-nitrobiphenyl follows the second generalization.

On the basis of resonance forms which can be written for 4-nitrobiphenyl the 2' and 4' positions are selectively deactivated and are relatively positive compared to the 3' positions. Consequently, attack by a positive nitronium ion at the 3' position might be expected to give the lowest energy transition state.
This, however, is not in accord with the observed formation of the 4,4' and 2,4' dinitrobiphenyls.

Electrophilic attack at the 2' and 4' positions offers the advantage that the intermediate or transition state can be stabilized by resonance interactions with the second ring.

\[
\begin{align*}
\text{[Diagram showing resonance structures]} & \end{align*}
\]

This is impossible with attack at the 3' position.

\[
\begin{align*}
\text{[Diagram showing resonance structures]} & \end{align*}
\]

However, it is important to stress, that this resonance interaction with the second ring removes electrons from an already electron deficient aromatic ring.

Since the position of attack resulting in the lowest activation energy is the favored one, then resonance stabilization of the 2' and 4' intermediate must override the positive-positive charge interaction of the second ring and produce a lower energy transition state than the 3' intermediate where no resonance interaction with the second ring can occur.
For resonance stabilization to occur in the biphenyls it is necessary that the two rings be coplanar. X-ray, dipole moment, spectra, and Kerr constants indicate 4-substituted biphenyls are planar in the crystalline state and planarity being the preferred configuration in solution. A Hammett correlation of 4'-substituted-4-biphenic acids and rate data on biphenyl substitution shows a substituent resonance and inductive interaction between the rings. This rate data, in conjunction with the other information substantiates resonance stabilization of the transition state by both rings.

The orientation found on nitration of 4,4'-dichlorobiphenyl and 2,2'-dichlorobiphenyl is indicative of the type of stabilization occurring in the transition state (Table II). Mononitration of 4,4'-dichlorobiphenyl occurs in the 2 position. Nitration of 2,2'-dichlorobiphenyl results in dinitration in the 3,3' positions. Since the coplanar 4,4'-dichlorobiphenyl allows resonance interaction between the two rings, the transition state at the two position gains additional stabilization from the second ring; this results in 2 substitution. However, in 2,2'-dichlorobiphenyl the rings are at an angle of 74° to one another and, therefore, little or no resonance interaction will occur between the rings. Orientation will now be directed by the stabilizing influence of the
TABLE II
REACTIONS OF SUBSTITUTED BIPHENYLS WITH CONTRASTED STERIC EFFECTS

\[ \text{Reaction 1: } \text{Cl}-\begin{array}{c} \text{HNO}_3 \to \\ & \text{Cl} \end{array}-\text{Cl} \rightarrow \begin{array}{c} \text{Cl} \end{array}-\begin{array}{c} \text{HNO}_3 \to \\ & \text{Cl} \end{array}-\text{Cl} + \begin{array}{c} \text{Cl} \end{array}-\begin{array}{c} \text{HNO}_3 \to \\ & \text{Cl} \end{array}-\text{Cl} \rightarrow <1\%
\]

\[ \text{Reaction 2: } \text{Cl}-\begin{array}{c} \text{HNO}_3 \to \\ & \text{Cl} \end{array}-\text{Cl} \rightarrow \begin{array}{c} \text{Cl} \end{array}-\begin{array}{c} \text{HNO}_3 \to \\ & \text{Cl} \end{array}-\text{Cl} + \begin{array}{c} \text{Cl} \end{array}-\begin{array}{c} \text{HNO}_3 \to \\ & \text{Cl} \end{array}-\text{Cl} \rightarrow \begin{array}{c} \text{Cl} \end{array}-\begin{array}{c} \text{HNO}_3 \to \\ & \text{Cl} \end{array}-\text{Cl} + \begin{array}{c} \text{Cl} \end{array}-\begin{array}{c} \text{HNO}_3 \to \\ & \text{Cl} \end{array}-\text{Cl} \rightarrow 80\%
\]

\[ \text{Reaction 3: } \text{Cl}-\begin{array}{c} \text{HNO}_3 \to \\ & \text{Cl} \end{array}-\text{Cl} \rightarrow \begin{array}{c} \text{Cl} \end{array}-\begin{array}{c} \text{HNO}_3 \to \\ & \text{Cl} \end{array}-\text{Cl} + \begin{array}{c} \text{Cl} \end{array}-\begin{array}{c} \text{HNO}_3 \to \\ & \text{Cl} \end{array}-\text{Cl} \rightarrow \begin{array}{c} \text{Cl} \end{array}-\begin{array}{c} \text{HNO}_3 \to \\ & \text{Cl} \end{array}-\text{Cl} + \begin{array}{c} \text{Cl} \end{array}-\begin{array}{c} \text{HNO}_3 \to \\ & \text{Cl} \end{array}-\text{Cl} \rightarrow 20\%
\]

Reference
16
17
TABLE II—Continued

Reference

<table>
<thead>
<tr>
<th>Chemical Structure 1</th>
<th>Chemical Structure 2</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Chemical Structure 1" /></td>
<td><img src="image2" alt="Chemical Structure 2" /></td>
<td>8</td>
</tr>
<tr>
<td><img src="image3" alt="Chemical Structure 1" /></td>
<td><img src="image4" alt="Chemical Structure 2" /></td>
<td>8</td>
</tr>
<tr>
<td><img src="image5" alt="Chemical Structure 1" /></td>
<td><img src="image6" alt="Chemical Structure 2" /></td>
<td>8</td>
</tr>
</tbody>
</table>
Cl group in the ring being substituted; this results in 3,3' disubstitution.

The same effect of resonance stabilization of the transition state is shown by the rates of chlorination of 2,2'-dimethylbiphenyl, 4,4'-dimethylbiphenyl and 3,3'-dimethylbiphenyl. The rate of chlorination of 2,2'-dimethylbiphenyl is comparable to toluene; 4,4'-' and 3,3'-dimethylbiphenyls chlorinate 20 and 500 times faster than toluene, respectively.15

These examples show that the transition state in biphenyls with deactivating groups, strongly interacts with the opposite ring unless this is prevented by steric effects. For a deactivating, normally meta directing group like nitro, this interaction with the second ring overrides normal effects and results in 4' substitution.

It has long been known,19 that strong electron interactions occur in certain reactions when applying Hammett correlations. This resulted in the formulation of the Brown treatment and the use of $\sigma^+$ constants for electrophilic aromatic substitution reactions.20

By the use of the Hammett plot of the ionization constants of biphenic acids\textsuperscript{14a} (see Graph I) it is possible to obtain the $\sigma$ values of the substituted phenyl group by considering the biphenic acids to be substituted benzoic acids (Table IV). Using these $\sigma$ values and Brown's conversion formula, the corresponding $\sigma^+$ values were
obtained and used to calculate isomer distributions and relative rates for electrophilic attack in substituted biphenyls.

In the case of 4-nitrobiphenyl the σ value as a substituted benzoic acid can be determined by finding the pKa of 4-nitrobiphenic acid corresponding to σ para nitro and reading the σ value for benzoic acids corresponding to that pKa. However, in this case the pKa was experimentally determined and that value was used to determine the σ value as a substituted benzoic acid. Experimentally determined values were used in all cases when available.

The σ⁺ values for the 4' and 3' positions were calculated using the relation given by Brown for aryl substituents.

\[
\begin{align*}
\sigma_p^+ &= \sigma_p - 0.13 & 1. \quad \sigma_{4'}^+ &= \sigma_{4}^- - 0.13 \\
\sigma_m^+ &= \sigma_m & 2. \quad \sigma_{3'}^+ &= \sigma_3
\end{align*}
\]

The σ⁺ values for the 2 and 3 positions were calculated assuming the effect of multiple substituents on the reactivity can be expressed by the Hammett equation in the form,

\[
\log \frac{K}{K_0} = \rho \Sigma \sigma
\]

and that the σ⁺ to σ relation of Brown still holds. Therefore it follows:

\[
\begin{align*}
3. \quad \sigma_2^+ &= \sigma_m^+ + \sigma_{4(H)}^+ \\
4. \quad \sigma_3^+ &= \sigma_p^+ + \sigma_{3(H)}^+
\end{align*}
\]
No steric correction was introduced for the 2 and 3 positions in calculating per cent substitution in these positions except for 4-methylbiphenyl. For deactivating groups the per cent substitution in the substituted ring was low without the introduction of a steric factor. In the cases of OCH$_3$ and NH$_2$, these groups are activating to such an extent that a steric factor would have made no significant difference in the isomer distribution. The per cent substitution in the 2' position is, however, experimentally about one-half the 4' value. The calculated values were therefore set to preserve the 2' to 4' ratio of one-half.

The isomer distributions are given for benzene derivatives by the relation:

$$c. \log \frac{D}{m} = \rho (\sigma^+_{p} - \sigma^+_{m}) - \log 2$$

Modification of the expression to accommodate the biphenyl system gives the following relation.

$$5. \log \frac{4'}{a} = \rho (\sigma^+_{4} - \sigma^+_{a}) - \log 2 \quad a = 3', 3, 2$$

To illustrate the use of these relations the expected isomer distribution on nitration of 4-methylbiphenyl will be calculated.
These are all the necessary $\sigma^+$ values for 4-methylbiphenyl to calculate the isomer distribution from equation 5. The only necessary information needed is the $\rho$ value for nitration. For aromatic nitration at 0°C. in acetic anhydride $\rho$ is -6.5.\textsuperscript{2,20} The ratio of 4' to 3' nitro derivative from equation 5 is 4.0.

$$\log \frac{4'}{3'} = \rho(\sigma^+_{4'} - \sigma^+_{3'}) - \log 2$$

$$\log \frac{4'}{3'} = -6.5(-.20 + .05) - .301$$
\[ \log \frac{4'}{3} = .674 \]

\[ \frac{4'}{3} = 10^{.674} = 4.0 \]

The ratio of 2' to 4' nitro derivative is set at 2 on steric considerations.

\[ \frac{4'}{2'} = 0.5 \]

The ratio of 4' to 2 nitro -4' methylbiphenyl is 2.4 x 10^{-1}.

\[ \log \frac{4'}{2} = \rho(\sigma^+_{4'} - \sigma^+_{2}) - \log 2 \]

\[ \log \frac{4'}{2} = -6.5(-.20 + .25) - .301 = -.626 \]

\[ \frac{4'}{2} = 10^{-.626} \times 10^{-1} = 2.4 \times 10^{-1} \]

If the same steric factor for 4' to 2' substitution is introduced the ratio becomes 9.6 x 10^{-1}.

\[ \frac{4'}{2} = 2.4 \times 10^{-1} \times 4 = 9.6 \times 10^{-1} \]

The ratio of 4' to 3 substitution is 4.2 x 10^{-1}.

\[ \log \frac{4'}{3} = \rho(\sigma^+_{4'} - \sigma^+_{3}) - \log 2 \]

\[ \log \frac{4'}{3} = -6.5(-.20 + .21) - .301 = -.366 \]

\[ \frac{4'}{3} = 10^{-.366} \times 10^{-1} = 4.3 \times 10^{-1} \]

The same steric factor found on nitration of toluene can be introduced here for the effect on the 4' to 3 ratio since the steric conditions are similar. The ortho to para ratio on nitration of toluene was found to be 1.57.²

With no steric effect the value for the ortho para ratio would be 2. The steric factor S is therefore given by the following relation.
\[
\frac{P_{\text{theoretical}}}{P_{\text{theoretical}}} \times S = \frac{P_{\text{actual}}}{P_{\text{actual}}}
\]

\[
S = \frac{1}{1.57}
\]

\[S = 1.27\]

Introducing this steric effect the ratio of 4' to 3' nitration becomes \(5.5 \times 10^{-1}\).

\[
\frac{4'}{3'} = 4.3 \times 10^{-1} \times 1.27 = 5.5 \times 10^{-1}
\]

This isomer distribution for substitution in the various positions can now be determined by solving the above ratios for per cent of 4' and calculating the others from that.

The isomer distribution neglecting all steric effects is:

<table>
<thead>
<tr>
<th>Per cent 4' = X</th>
<th>1.00 X</th>
<th>10% - 4'</th>
</tr>
</thead>
<tbody>
<tr>
<td>3' = .25(4')</td>
<td>.25 X</td>
<td>3% - 3'</td>
</tr>
<tr>
<td>2' = 2(4')</td>
<td>2.00 X</td>
<td>21% - 2'</td>
</tr>
<tr>
<td>2 = 4.16(4')</td>
<td>4.16 X</td>
<td>43% - 2</td>
</tr>
<tr>
<td>3 = 2.32(4')</td>
<td>2.32 X</td>
<td>24% - 3</td>
</tr>
</tbody>
</table>

\[9.73 X = 100\]

\[X = 10.3\]

The isomer distribution correcting for all steric effects is:

<table>
<thead>
<tr>
<th>4' = X</th>
<th>1.00 X</th>
<th>22% - 4'</th>
</tr>
</thead>
<tbody>
<tr>
<td>3' = .25(4')</td>
<td>.25 X</td>
<td>5% - 3'</td>
</tr>
<tr>
<td>2' = .5(4')</td>
<td>.50 X</td>
<td>11% - 2'</td>
</tr>
<tr>
<td>2 = 1.04(4')</td>
<td>1.04 X</td>
<td>23% - 2</td>
</tr>
<tr>
<td>3 = 1.82(4')</td>
<td>1.82 X</td>
<td>39% - 3</td>
</tr>
</tbody>
</table>

\[4.61 X = 100\]

\[X = 21.7\]
The data for calculated isomer distribution is contrasted to experimental findings in Table III. The general agreement of the data further substantiates that the strong electron interaction in normal aromatic substitution occurs in both rings of the biphenyls and is responsible for the position of attack.

The Brown equation applied to biphenyls actually predicts 4-nitrobiphenyl should undergo electrophilic attack in the 4' position. By applying these calculations it can be said generally - if the \( \sigma^+ \) value of the \( X-O^- \) group of biphenyl is more negative than \( \Sigma \sigma^+ \) values of phenyl and the group \( X \), direction will be ortho, para in the unsubstituted ring. This is the result for deactivating groups.

If the \( \Sigma \sigma^+ \) values of \( X-O^- \) and phenyl becomes more positive than \( \sigma^+ \) for group \( X \), attack takes place in the substituted ring. This occurs when \( X \) is a strong electron donating group. This is the observed result for electron donating groups with the exception of \(-NH^R\) under highly acidic conditions (Table I).

In the case of the \(-NHCOR\) group substitution takes place in the 4' position under highly acidic conditions and in the 3 position under weakly acidic or neutral conditions.\(^{22,23}\) This is best rationalized by considering attack taking place on the \( O-O^-NH^{CR} \) molecule under
TABLE III

COMPARISON OF CALCULATED AND EXPERIMENTAL ISOMER DISTRIBUTIONS
FOR NITRATION OF SUBSTITUTED BIPHENYLS

\[
\begin{array}{ccc}
\text{X} & \text{HNO}_3 & \text{NO}_2 \\
3 & 2 & 2' & 3' & 4' & 3' & 2' & 2 & 3 \\
\end{array}
\]

<table>
<thead>
<tr>
<th>Substituent X</th>
<th>Calculated % Nitrations in Position</th>
<th>Experimental % Nitrate: in Position</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4'</td>
<td>3'</td>
</tr>
<tr>
<td>NO₂</td>
<td>53</td>
<td>20</td>
</tr>
<tr>
<td>CHO</td>
<td>61</td>
<td>8</td>
</tr>
<tr>
<td>COOH</td>
<td>60</td>
<td>11</td>
</tr>
<tr>
<td>Cl</td>
<td>61</td>
<td>8</td>
</tr>
<tr>
<td>H</td>
<td>66</td>
<td>2</td>
</tr>
<tr>
<td>CH₃</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Steric</td>
<td>22</td>
<td>5</td>
</tr>
<tr>
<td>OCH₃</td>
<td>&lt; 1</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Chlorination</td>
<td>&lt; 1</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>NH₂</td>
<td>&lt; 1</td>
<td>&lt; 1</td>
</tr>
</tbody>
</table>

Chlorination

Bromination
<table>
<thead>
<tr>
<th>Group</th>
<th>Sigma and Sigma Plus Values in Benzene Derivatives</th>
<th>Sigma and Sigma Plus Values in Biphenyl Derivatives</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\sigma^a_p$, $\sigma^b_p$, $\sigma^c_p$, $\sigma^a_m$, $\sigma^b_m$, $\sigma^c_m$</td>
<td>$\sigma^d_4$, $\sigma^e_3$, $\sigma^d_4$, $\sigma^e_3$, $\sigma^e_4$, $\sigma^e_3$, $\sigma^f_2$, $\sigma^f_3$</td>
</tr>
<tr>
<td>NO$_2$</td>
<td>.778, .65, .79, .710, .71, .674</td>
<td>.24, .22, .11, .22, .50, .89</td>
</tr>
<tr>
<td>CHO</td>
<td>.216, .09, - , .355, .36, -</td>
<td>.05, .10, -.08, .10, .30, .19</td>
</tr>
<tr>
<td>COOH</td>
<td>.265, .13, .421, .355, .36, .322</td>
<td>.07, .10, -.06, .10, .14, .52</td>
</tr>
<tr>
<td>H</td>
<td>.000, .00, .000, .000, .000, .000</td>
<td>.08, (.06)$^c$, (.103)$^c$, (.179)$^c$, (.10)$^c$, (.179)$^c$, (.10)$^c$</td>
</tr>
<tr>
<td>Cl</td>
<td>.227, .10, .114, .373, .37, .399</td>
<td>.09, .105, -.04, .105, .22, .22</td>
</tr>
<tr>
<td>Br</td>
<td>.232, .10, .150, .391, .391, .405</td>
<td>.09, .11, -.04, .11</td>
</tr>
<tr>
<td>CH$_3$</td>
<td>-.170, -.30, -.311, -.069, -.069, -.066</td>
<td>-.07, -.05, -.20, -.05, -.245, .208</td>
</tr>
<tr>
<td>OCH$_3$</td>
<td>-.268, -.40, -.778, -.115, -.12, .047</td>
<td>-.11, .04, -.24, -.04, -.132, .68</td>
</tr>
</tbody>
</table>

$^a$See Ref. 21. Values given by Jaffe.
$^b$Calculated from equations a and b.
$^c$Values given by Brown, Ref. 20.
$^d$Determined from Graph I.
$^e$Determined by equations 1 and 2.
$^f$Determined by equations 3 and 4.
GRAPH I

HAMMETT CORRELATION FOR BENZOIC AND BIPHENIC ACIDS$^{14a}$

Biphenic Acids $\rho = +.49$

Benzoic Acids $\rho = +1.32$
weakly acidic conditions. The group being activating directs attack to the 3 position in the substituted ring. Under highly acidic conditions the protonated molecule is probably attacked. The protonated species being less activating directs to the unsubstituted ring.

A similar case for the nitration of acetanilide under acidic conditions might be shown as,

\[
\begin{align*}
\text{NHCCCH}_3 \quad &\xrightarrow{H^+} \quad \text{NHCCCH}_3 \quad \xrightarrow{\text{NO}_2^+} \quad \text{NHCCCH}_3 \\
\text{NHCCCH}_3 \quad &\xrightarrow{\text{NO}_2^+} \quad \text{NHCCCH}_3
\end{align*}
\]

since acetanilide is almost completely protonated under highly acidic conditions.\(^{24}\)

This reaction sequence necessitates placing adjacent positive charges on the resonance stabilized intermediate A. This is analogous to the situation arising in order to explain why styrenes with deactivating groups in the \(\beta\) position undergo nitration in the ortho and para positions.\(^{25,26,27}\)

For the \(\beta\) substituted styrenes whose substituent is normally meta directing the resonance considerations are analogous to the biphenyls. In this system, however, only one additional resonance form contributes to the
stabilization in the ortho and para positions and that resonance form involves having positive charges on adjacent atoms.

\[
\begin{align*}
\text{\textbf{N}} & \text{O}^- \\
\text{\textbf{C}} & \text{\textbf{C}} \\
\text{\textbf{C}} & \text{\textbf{C}} \\
\end{align*}
\]

Although resonance forms having adjacent positive charges are generally considered high energy forms and small contributors to the overall stabilization of the molecule, this in no way means this type contribution is impossible. In the \(N_2O_4\) molecule two bonded nitrogen atoms each having a formal plus-one charge exist in a relatively stable molecule.

Similar calculations to those of biphenyl orientation using \(\sigma^+\) values (Table VI) indicate the position of attack to be ortho and para in the \(\beta\) substituted styrene. As in the biphenyls, in this system interaction with the double bond of styrene stabilizes the intermediate in electrophilic aromatic substitution.

For the \(\beta\) substituted styrenes the values of \(\sigma\) were calculated from the ionization constants of appropriate trans-3-substituted acrylic acids.\(^{28}\) The \(\rho\) value was calculated for the acids in Table V by the least squares method. The assumption made is that the \(\rho\) value of the \(\beta\) substituted styrenes, the value of which has not been
determined, is equal to the $p$ value of the trans-3-substituted acrylic acids.\(^{21}\) Therefore, the $\sigma$ values for the acrylic acids can be used to determine the difference in $\sigma^+$ values for the para and meta positions in the $\beta$ substituted styrenes. The $(\sigma^+_p - \sigma^+_m)$ values are listed in Table VI. Other $\sigma$ and $\sigma^+$ values are not given since they are likely to be in error by some constant difference due to the effect of the environmental difference of the carboxyl group in the acrylic acid derivatives compared to the benzoic acid derivatives.

The $\sigma$ values to be used in order to get the value of $(\sigma^+_p - \sigma^+_m)$ for the $\beta$ substituted styryl group can be read from graph II or given by the relation\(^{19}\)

$$\log \frac{K_X}{K_H} = \sigma \quad K_H = \text{benzoic acid}$$

These $\sigma$ values can then be used in equations a and b to calculate the $\sigma^+$ values for the para and meta positions. Of course these values are inaccurate without the environmental factor. The difference of the $\sigma^+_p$ and $\sigma^+_m$ is taken. The environmental factor eliminated, this difference can be used in equation c to determine the expected isomer distribution.

As for the biphenyls the per cent substitution in the ortho position was set at one-half the para value to agree with the experimental steric factor. The values calculated contrasted with experimental values are given in Table V.
The trans-3-substituted acrylic acids chosen are better named substituted cinnamic acids.
TABLE V
DISSOCIATION CONSTANTS AND pKa'S OF THE SUBSTITUTED CINNAMIC ACIDS OF GRAPH II

<table>
<thead>
<tr>
<th>Group</th>
<th>Dissociation Constant $10^5$ K in H$_2$O at 25°C.</th>
<th>pKa</th>
</tr>
</thead>
<tbody>
<tr>
<td>p-NO$_2$</td>
<td>8.99</td>
<td>4.048</td>
</tr>
<tr>
<td>m-NO$_2$</td>
<td>7.58</td>
<td>4.120</td>
</tr>
<tr>
<td>p-Cl</td>
<td>3.86</td>
<td>4.414</td>
</tr>
<tr>
<td>H</td>
<td>3.65</td>
<td>4.438</td>
</tr>
<tr>
<td>p-CH$_3$</td>
<td>2.73</td>
<td>4.564</td>
</tr>
<tr>
<td>p-OCH$_3$</td>
<td>2.89</td>
<td>4.534</td>
</tr>
</tbody>
</table>

TABLE VI
COMPARISON OF CALCULATED AND EXPERIMENTAL ISOMER DISTRIBUTIONS FOR NITRATION OF β SUBSTITUTED STYRENES

<table>
<thead>
<tr>
<th>β-substituent</th>
<th>$\sigma_p^+ - \sigma_m^+$</th>
<th>Per cent Nitrination Calculated</th>
<th>Isomer Distribution Found</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>o m p</td>
<td>o m p</td>
<td></td>
</tr>
<tr>
<td>NO$_2$</td>
<td>-.06</td>
<td>22 35 43</td>
<td>31 2 67</td>
<td>25</td>
</tr>
<tr>
<td>N(CH$_3$)$_3$</td>
<td>-.15</td>
<td>30 12 59</td>
<td>34 3 61</td>
<td>26</td>
</tr>
<tr>
<td>COOH</td>
<td>-.18</td>
<td>31 8 61</td>
<td>only o, p</td>
<td>27</td>
</tr>
</tbody>
</table>
In most cases the calculated isomer distributions show an acceptable relation to the experimentally found results. This agreement seems to show a relative accuracy of $\sigma_p^+$ to $\sigma_m^+$ values calculated. This agreement also indicates the $-.13$ factor used in calculating $\sigma^+$ values is operative in electrophilic attack in biphenyls and a strong interaction with the second ring is responsible for the observed orientation in biphenyls and interaction with the double bond in $\beta$ substituted styrenes responsible for ortho para substitution in that system.

One way to prove that resonance with the second ring in biphenyls and with the double bond in $\beta$ substituted styrenes is responsible for the ortho para orientation is to remove the two rings from conjugation in the biphenyls and to remove the double bond from resonance in the $\beta$ substituted styrenes and determine the effect on rate of electrophilic attack and the position of attack.

For biphenyl this is an easy procedure, for 2-trimethylarsonium-3' -bromobiphenyl iodide has been prepared and resolved. Therefore, preparing the completely hindered 2-trimethylarsoniumbiphenyl iodide and the unhindered 4-trimethylarsoniumbiphenyl iodide, measuring their relative rates of nitration and determining the position of nitration would contrast the rate and orientation effects in a non-conjugated and conjugated
biphenyl with a normally deactivating meta directing group. The expected result would be for 2-trimethylarsoniumbiphenyl to nitrate slower than the 4' derivative and to be attacked and substitute in the 3' position while for 4-trimethylarsoniumbiphenyl to substitute in the 4' and 2' positions.

A similar set of experiments for the two compounds below should demonstrate the effect of the double bond in the orientation of styrenes with a deactivating group in the 8 position.

The expected result for electrophilic attack on A would be substitution ortho and para in ring one at a rate faster than B. For B substitution should occur in the meta position of ring 2.
REFERENCES


7. de la Mare, P. B. D., and Ridd, J. H., *op. cit.*, Chapter 11.


15. de la Mare, P. B. D., Hall, Muriel D., Harris, Margaret M., and Hassan, M., Chem. and Ind., 1086 (1958).


