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# The Substituent Effect. 15.$^{1)}$ The LSFE Treatment of Substituent Effects on Basicities of Pyridines$^{2)}$

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The relative dissociation constants of meta and para substituted pyridinium ions in $H_2O$ at 25 °C were collected from a number of sources. To understand the actual substituent effects with a combination of inductive(*I*) and pi-electronic(*Pi*) effect components, the LSFE equation has been employed statistically for each of the meta and para series.

$$\Delta pK_a = \rho_i\sigma_i + \rho_\pi^+\sigma_\pi^+ + \rho_\pi^-\sigma_\pi^-$$

The results illustrate (1) the *I* effect from the meta position is 1.2 times more effective than that from the para position, (2) the *Pi* effects from the para position have clearly different sensitivities for pi-donor($-R$) and pi-acceptor($+R$) classes of substituents; more exalted and more reduced *Pi* effects than that involved in $\sigma_p^\circ$ constants for $-R$ and $+R$ groups, respectively. Compared with earlier results from the Taft's DSP and relevant treatments, the soundness of the dual $\rho_\pi$ approach and, further, the superiority of the LSFE treatment have been demonstrated for the description of substituent effects on basicity changes in pyridines.

Substituent effects on benzene reactivities have been most widely handled with a combination of two components, polar (inductive, *I*) and resonance (pi-electronic, *Pi*) effects, each of which is given as a $\rho\sigma$ product.$^{1,3,4)}$ In an attempt to justify this treatment, the analysis of substituent effects in the extended pi-electron system of naphthalene has been discussed previously.$^{1,4f)}$ The same treatment should be applicable to reactivities in heteroaromatic pi-electron systems.

Meta and para substituted pyridines are an interesting system for an application of the separation analysis in heteroaromatic reactivities. For basicities of pyridines, certain contradictions have recently appeared in the rationalization of the substituent effects obtained from different equations.$^{5,6)}$ The validity of an equation may be tested most critically by establishing whether or not the substituent effects on reactivities in pyridines can be treated successfully. In this sense, Taft and coworkers have stressed the power of the DSP treatment$^{4a)}$ mainly on the basis of the following two facts:$^{5)}$ (i) the $\sigma_R^+$ parameter gives the best-fit DSP correlation, as anticipated from a structural point of view; (ii) the resultant $\rho_I$ is essentially identical with the $\rho_I$ for the corresponding saturated system, the 4-substituted quinuclidines.$^{7)}$

$$(\Delta pK_a)_{py}^{p} = 5.15\sigma_I + 2.69\sigma_R^+ \qquad (1)$$

$$(\Delta pK_a)_{py}^{p} - (\Delta pK_a)_{qu}^{4} = 2.87\sigma_R^+ \qquad (2)$$

The latter point is particularly notable, since it is in line with the relationship between benzoic acid and bicyclo[2.2.2]octane-1-carboxylic acid.$^{8)}$

Johnson *et al.* have interpreted the pi-donor para substituent effects using Eq. 3, based on the assumption that substituent effects of para pi-acceptors are exclusively inductive.$^{6,9)}$

$$\begin{aligned}(\Delta pK_a)_{py}^{p} &= 5.66\sigma \text{ (for pi-donors) and}\\ &\quad 5.66\sigma_I \text{ (for pi-acceptors);}\\ (\Delta pK_a)_{py}^{p} - 1.19\ (\Delta pK_a)_{qu}^{4} &= 5.66\sigma_R\\ &\quad \text{(for pi-donors)} \qquad (3)\end{aligned}$$

They argued that the correlation with $\sigma_R$ parameters (instead of $\sigma_R^+$) cast doubt on the validity of the DSP and, generally, of multiple substituent parameter treatments,$^{6)}$ including our LArSR treatment. Thus, using the same data sets for pyridines and quinuclidines, different authors have reached conflicting conclusions on the significance of the DSP treatment.

We have demonstrated the applicability and the validity of the LSFE Eq. 4 through appropriate separation of substituent effects in various aromatic hydrocarbon systems as well as in the ordinary benzene system.$^{1)}$

$$\log k/k_0 = \rho_i\sigma_i + \rho_\pi^+\sigma_\pi^+ + \rho_\pi^-\sigma_\pi^- \qquad (4)$$

In the present study, we apply Eq. 4 to the analysis of substituent effects on the basicity of pyridines and provide evidence for the significance of the dual $\rho_\pi$ approach for pi-donor and pi-acceptor substituents characteristic of our LSFE treatment, Eq. 4. The results provide a solution to the above controversial problem on the DSP treatment and characterize the LSFE treatment as a precise and useful equation for the separation analysis of actual substituent effects.

## Results and Discussion

A number of reliable $\Delta pK_a$ values have been collected from various sources (Table 1). The $\Delta pK_a$ values were defined by $pK_H - pK_X$, where both data were determined by the same authors and under the same experimental conditions, unless otherwise noted. From examination of earlier compilations, together with some additional fragmentary data, best values were selected and are listed in the last column of Table 1. The data set consists mostly of Fischer's results, but for alkyl and nitro substituents, Brown's and Bellobono's data were employed, since, for the alkyl substituents, meta and para data were available as a pair, and, for the nitro substituent, Fischer's value was much lower than that reported by the other two authors. A full set of basicity data has been constructed for a total of 52 meta and para substituents.$^{20)}$

The present data set for the basicities of pyridines

TABLE 1. DATA OF $\Delta pK_a$ OF SUBSTITUTED PYRIDINIUM IONS IN $H_2O$ AT 25 °C[a)]

| Subst | Brown[10)]<br>Bryson[11)] | Jaffe[12)] | Schofield[15)] | Fischer[9b)] | Bellobono[16)] | Taft[5a,17)] | Arnett[18)]<br>others | Best selected[b)] |
|---|---|---|---|---|---|---|---|---|
| H | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| 3-Me | (−0.53)<br>0.41<br>−0.51[10)]<br>−0.34 | −0.53<br>(−0.51) | −0.51 | $-\underline{0.46}$ | | (−0.46) | −0.51<br>−0.45 | −0.46 |
| 4-Me | −0.85[10)] | (−0.85) | | $-\underline{0.82}$ | | (−0.82) | −0.85<br>−0.79 | −0.82 |
| 3-Et | $-\underline{0.53}$[10)] | (−0.53) | −0.51 | | | | | −0.53 |
| 4-Et | $-\underline{0.85}$[10)] | (−0.85) | | −0.82 | | (−0.85) | | −0.85 |
| 3-*i*-Pr | $-\underline{0.55}$[10)] | (−0.55) | −0.59 | | | | | −0.55 |
| 4-*i*-Pr | $-\underline{0.85}$[10)] | (−0.85) | | −0.83 | | (−0.85) | | −0.85 |
| 3-*t*-Bu | $-\underline{0.65}$[10)] | (−0.65) | | | | | | −0.65 |
| 4-*t*-Bu | $-\underline{0.82}$[10)] | (−0.82) | | | | (−0.82) | | −0.82 |
| 3,5-Me$_2$ | −0.93 | | −0.94 | $-\underline{0.93}$ | | | −1.01 | −0.93 |
| 3,4-Me$_2$ | | | | $-\underline{1.27}$ | | | | −1.27 |
| 4-*n*-Pr | | | | $-\underline{0.84}$ | | | | −0.84 |
| 3-F | $\underline{2.20}$[10)] | (2.20) | | | | 2.24 | | 2.20 |
| 3-Cl | 2.33[10)] | (2.33) | | $\underline{2.40}$ | | (2.40) | | 2.40 |
| 4-Cl | | 1.45 | | $\underline{1.38}$ | | (1.38) | | 1.38 |
| 3-Br | 2.33[10)] | (2.33) | 2.33 | $\underline{2.36}$ | 2.49 | (2.36) | | 2.36 |
| 4-Br | | | | $\underline{1.46}$ | 1.53 | (1.46) | | 1.46 |
| 3-I | $\underline{1.92}$[10)] | (1.92) | | | | 1.96 | | 1.92 |
| 4-I | | | | | | *ca.* 1.19* | | *ca.* 1.2 |
| 3,5-Cl$_2$ | | | | $\underline{4.54}$ | | | | 4.54 |
| 3,5-Br$_2$ | | | | $\underline{4.39}$ | | | | 4.39 |
| 3-OMe | 0.27 | 0.35* | | $\underline{0.43}$ | | 0.30 | | 0.43 |
| 4-OMe | | −1.39* | | $-\underline{1.37}$ | | (−1.37) | | −1.37 |
| 3-OH | (0.43) | 0.43 | | | | 0.41 | | *ca.* 0.4 |
| 3-SMe | | $\underline{0.78}$*[14)] | | | | (0.78*) | | 0.78* |
| 4-SMe | | $-\underline{0.74}$*[14)] | | | | (−0.74*) | | −0.74* |
| 3-NH$_2$ | (−0.80)[12)] | (−0.86*)[10)] | | $-\underline{0.83}$ | −0.82<br>−0.80 | (−0.83) | | −0.83 |
| 4-NH$_2$ | | −3.94* | −3.93 | $-\underline{3.91}$ | −3.94 | (−3.91) | | −3.91 |
| 3-NMe$_2$ | | | | | | | $-\underline{1.16}$[19)] | −1.16 |
| 4-NMe$_2$ | | | $-\underline{4.36}$ | | | (*ca.* −4.49*) | | −4.36 |
| 3-NHAc | | $\underline{0.77}$* | | | | 0.84 | | 0.77* |
| 4-NHAc | | $-\underline{0.64}$* | | | | *ca.* −0.66 | | −0.64* |
| 3-NHCOPh | | $\underline{1.43}$* | | | | | | 1.43* |
| 4-NHCOPh | | $-\underline{0.09}$* | | | | | | −0.09* |
| 3-Ph | | | | | | *ca.* 0.41 | | *ca.* 0.4 |
| 4-Ph | | | | $-\underline{0.14}$ | | (−0.14) | | −0.14 |
| 4-PhCH$_2$ | | | | $-\underline{0.38}$ | | (−0.38) | | −0.38 |
| 3-COPh | | | | $\underline{2.03}$ | | (2.03) | | 2.03 |
| 4-COPh | | | | $\underline{1.86}$ | | (1.86) | | 1.86 |
| 3-CN | (3.84) | 3.84 | | $\underline{3.86}$ | 4.04 | (3.86) | | 3.86 |
| 4-CN | | | | $\underline{3.35}$ | 3.73 | (3.35) | | 3.35 |
| 3-NO$_2$ | 4.36 | (4.42)[11,13)] | | 4.03 | $\underline{4.42}$ | (4.03) | | 4.42 |
| 4-NO$_2$ | | | 3.62 | 3.82 | $\underline{3.98}$ | (3.82) | | 3.98 |
| 3-COMe | 1.99[10)] | (1.99) | | | | 2.03 | $\underline{1.95}$ | 1.95 |
| 4-COMe | | | | $\underline{1.70}$ | | (1.70) | 1.70 | 1.70 |
| 3-CONH$_2$ | | *ca.* 1.72* | | | | | | *ca.* 1.7* |
| 4-CONH$_2$ | | *ca.* 1.51* | | | | | | *ca.* 1.5* |
| 3-COOMe | | | | $\underline{2.12}$ | | (2.12) | | 2.12 |
| 4-COOMe | | | | $\underline{1.72}$ | | (1.72) | | 1.72 |
| 4-CF$_3$ | | | | | | $\underline{2.58}$ | | 2.58 |
| 3-COO$^-$ | 0.45 | *ca.* 0.52 | | $\underline{0.45}$ | | | | 0.45 |
| 4-COO$^-$ | | *ca.* 0.39 | | $\underline{0.31}$ | | | | 0.31 |

a) Values in brackets are from another column. b) An underlined value is chosen as the best selected value.
*) Data at 20 °C.

Table 2. Apparent $\sigma$ and related values

| Subst | $\bar{\sigma}_{\text{py}}$[a)] | $\sigma^{\circ}$[b)] |
|---|---|---|
| H | 0.000 | 0.000 |
| 3-Me | −0.063 | −0.069 |
| 4-Me | −0.120 | −0.124 |
| 3-Et | −0.074 | −0.07 |
| 4-Et | −0.125 | −0.131 |
| 3-*i*-Pr | −0.077 | −0.07 |
| 4-*i*-Pr | −0.125 | −0.156 |
| 3-*t*-Bu | −0.093 | −0.10 |
| 4-*t*-Bu | −0.120 | −0.174 |
| 3-F | 0.364 | 0.337 |
| 3-Cl | 0.396 | 0.373 |
| 4-Cl | 0.232 | 0.281 |
| 3-Br | 0.389 | 0.391 |
| 4-Br | 0.245 | 0.296 |
| 3-I | 0.319 | 0.352 |
| 4-I | *ca.* 0.20 | 0.26 |
| 3-OMe | 0.080 | 0.115 |
| 4-OMe | −0.208 | −0.100 |
| 3-OH | *ca.* 0.08 | 0.12 |
| 3-SMe | 0.136* | 0.12 |
| 4-SMe | −0.107* | 0.07 |
| 3-$NH_2$ | −0.122 | −0.15 |
| 4-$NH_2$ | −0.615 | −0.36 |
| 3-$NMe_2$ | −0.175 | −0.15 |
| 4-$NMe_2$ | −0.688 | −0.43 |
| 3-NHCOMe | 0.135* | 0.12 |
| 4-NHCOMe | −0.091* | 0.00 |
| 3-NHCOPh | 0.240* | 0.22 |
| 4-NHCOPh | −0.003* | 0.08 |
| 3-Ph | *ca.* 0.08 | |
| 4-Ph | −0.011 | 0.039 |
| 3-COMe | 0.324 | 0.376 |
| 4-COMe | 0.284 | 0.491 |
| 3-$CONH_2$ | *ca.* 0.28* | 0.32 |
| 4-$CONH_2$ | *ca.* 0.25* | 0.38 |
| 3-COOMe | 0.351 | 0.36 |
| 4-COOMe | 0.287 | 0.46 |
| 4-$CF_3$ | 0.425 | 0.505 |
| 3-COPh | 0.336 | 0.35 |
| 4-COPh | 0.309 | 0.49 |
| 3-CN | 0.630 | 0.615 |
| 4-CN | 0.548 | 0.653 |
| 3-$NO_2$ | 0.719 | 0.710 |
| 4-$NO_2$ | 0.649 | 0.800 |

*) Data at 20 °C. a) Calcd by using $\rho_m = 6.24$ (see text). b) Taken from Ref. 3b: original references cited therein.

Table 3. Substituent constants used in the LSFE analysis[a)]

| Subst | $\sigma_I$ | $\sigma_R^+$ | $\sigma_R^-$ |
|---|---|---|---|
| H | 0.000 | 0.000 | 0.00 |
| Me | −0.045 | −0.078 | 0.00 |
| Et | −0.045 | −0.069 | 0.00 |
| *i*-Pr | (−0.053)[b)] | (−0.051)[b)] | 0.00 |
| *t*-Bu | (−0.060)[b)] | (−0.034)[b)] | 0.00 |
| F | 0.363 | −0.118 | 0.00 |
| Cl | 0.348 | −0.070 | 0.00 |
| Br | 0.337 | −0.061[c)] | 0.00 |
| I | (0.289)[b)] | (−0.068)[b)] | 0.00 |
| OMe | 0.185 | −0.281 | 0.00 |
| OH | 0.19 | −0.34 | 0.00 |
| SMe | (0.17)[b)] | (−0.285)[b)] | 0.00 |
| $NH_2$ | 0.10[c)] | −0.46[c)] | 0.00 |
| $NMe_2$ | 0.11[c)] | −0.54 | 0.00 |
| Ph | 0.110 | −0.090 | 0.12 |
| COPh | 0.20 | 0.000 | 0.28 |
| $CONH_2$ | *ca.* 0.20 | 0.000 | 0.175 |
| COOMe | 0.23 | 0.000 | 0.22 |
| COMe | 0.214 | 0.000 | 0.266 |
| $CF_3$ | 0.34 | 0.000 | 0.143 |
| CN | 0.42 | 0.000 | 0.226 |
| $NO_2$ | 0.46 | 0.000 | 0.332 |

a) Data taken from Refs. 22 and 23. b) Not confirmed yet. See Ref. 3b. c) Calcd by 0.415 $\Delta\bar{\sigma}_R^+$. The $\Delta\bar{\sigma}_R^+$ value of *p*-$NH_2$ was redetermined most recently as −1.10.[24)]

is comparable in size with that of $\Delta pK_a$ for benzoic acids, and shows large substituent effects ($\rho \simeq 6$)[9b)] particularly useful for analysis of the substituent effects in detail. Since the solvent is water, it is not necessary to consider solvent modification of substituent constants.[3b)]

A least squares calculation gives a linear relation of $\Delta pK_a$ with $\sigma_m$ for meta substituents ($n=20$) with high precision.[21)]

$$(\Delta pK_a)_{\text{py}}^{m} = 6.240\sigma_m - 0.070 \qquad (5)$$

Based on this correlation, apparent $\bar{\sigma}$ values for the pyridine system ($\bar{\sigma}_{\text{py}}$) are evaluated as $(\Delta pK_a + 0.07)/6.24$ in the same way as in the benzene reactivities (Table 2). In order to shed further light on the substituent effects in the pyridine system, it is appropriate to examine the application of LSFE Eq. 4 to the same data set.

As suggested by Taft, the reliability of any multiparameter correlation depends upon the spread of the values of substituent constants as well as on the non-linearity between the two sets of substituent constants.[4a)] The present set covers a sufficiently wide range of substituents whose $\sigma_I$ and $\sigma_R$ values, given in Table 3, are scattered widely in an independent manner. In the present analysis, SMe, I, and $NHCOC_6H_5$ substituents were not included, since the substituent constants have not yet been well established. For alkyl groups, only methyl and ethyl groups were included as representative alkyls to prevent too much weight being attached to this class of substituents.

Table 4 summarizes the results of the LSFE analysis,[1,3,22–25)] together with those of the relevant Taft DSP[4a,5)] and of Johnson's[6)] treatments. Examination of the LSFE correlation results reveals the following important facts.

(1) The LSFE Eq. 4 applies both for para and meta series in the present system with excellent precision comparable to that for correlations in the benzene system.

Table 4. Correlation parameters by means of LSFE and DSP treatments

| Treatment | Position | Correlation parameters with substituent constants[a)] | Corr. coeff. | SD | Substituents included |
|---|---|---|---|---|---|
| LSFE | para | $6.49\sigma_i+9.50\sigma_\pi^++2.20\sigma_\pi^--0.03$ | 0.9972 | 0.175 | Me, Et, Cl, Br, OMe, $NH_2$, $NMe_2$, Ph, H, $CF_3$, COMe, CN, $NO_2$, COPh, COOMe. |
| LSFE | meta | $7.67\sigma_i+3.62\sigma_\pi^++2.03\sigma_\pi^-+0.01$ | 0.9974 | 0.123 | Me, Et, F, Cl, Br, OMe, $NH_2$, $NMe_2$, H, COMe, CN, $NO_2$, COPh, COOMe. |
| DSP | para | $5.28\sigma_I+2.71\sigma_R^+-0.03$ | 0.9987 | 0.120 | Me, Cl, Br, OMe, $NH_2$, $NMe_2$, Ph, H, $CF_3$, COMe, CN, $NO_2$, COOMe. |
| DSP | para | $5.45\sigma_I+4.92\sigma_R(BA)-0.26$ | 0.9944 | 0.259 | Me, Cl, Br, OMe, $NH_2$, $NMe_2$, Ph, H, $CF_3$, COMe, CN, $NO_2$, COOMe. |
| DSP | meta | $6.40\sigma_I+2.69\sigma_R^\circ-0.09$ | 0.9975 | 0.124 | Me, F, Cl, Br, OMe, $NH_2$, $NMe_2$, H, COMe, CN, $NO_2$, COOMe. |
| Johnson's[b)] | para | $5.69\sigma_X+0.10$ | 0.9979 | 0.172 | Me, Cl, Br, OMe, $NH_2$, $NMe_2$, Ph, H, $CF_3$, COMe, CN, $NO_2$, COOMe. |

a) The numerical values for the DSP treatment are taken from Ref. 4a. b) $\sigma_X=\sigma_I+\sigma_R(BA)$ for pi-donor substituents and $\sigma_X=\sigma_I$ for pi-acceptors.

(2) In the para correlation, the $\rho_\pi^+$ value differs from the $\rho_\pi^-$; the $\rho_\pi^+$ is higher than, but the $\rho_\pi^-$ is significantly lower than, the $\rho_i$ value. Note that in our LSFE Eq. 4, $\rho_i=\rho_\pi^+=\rho_\pi^-$ or $\rho_\pi^+/\rho_i=\rho_\pi^-/\rho_i=1.00$ refers by definition to the benzene $\sigma_p^\circ$ set.[1,3,22–25)] Neither the ratio $\rho_\pi^+/\rho_i$ nor $\rho_\pi^-/\rho_i$ is equal to unity in the present case, but the former $(=1.5)$ is comparable to that of 1.6 for the $\sigma_p$ constant,[26)] and the latter is much lower than that of 1.0 for the $\sigma_p^\circ$ constant. The ratio of $\rho_\pi^+/\rho_\pi^-$ $(=4)$ is comparable to that for the $\sigma_p^+$ constant.[26)]

(3) In the meta series, $\rho_\pi^+\simeq\rho_\pi^-$ is approximately satisfied and both $\rho_\pi^+/\rho_i$ and $\rho_\pi^-/\rho_i$ give essentially the same value of 0.4, which is comparable to the ratio in the benzene $\sigma_m$ constant.[26)] It is worthy of note that the $\rho_\pi^-$ value for the para pi-acceptor series is comparable to either $\rho_\pi^-$ or $\rho_\pi^+$ for the meta series.

(4) The ratio of the inductive components in the meta and para substituent effects, $\rho_i^m/\rho_i^p$, is found to be 1.18, which is virtually identical with the corresponding ratio 1.17 in the benzene system. Based on $\sigma_i^m=1.17\sigma_i^p$ as in the benzene reactivity, the $\rho_m$ value can be given as 6.5. This lends some support to the basic assumption of Hammett-type treatments; $\rho_m=\rho_p$ is as valid for the pyridine system as for the benzene system.

It is clear from (2) that the effect of pi-donor substituents at the para position is not significantly exalted relative to $\sigma_p^\circ$ and that the effect of pi-acceptors consists of a minor *Pi* effect. This is further suggested by the LArSR correlation for the present system (corr. coeff., 0.996 and standard deviation, ±0.21):

$$(\Delta pK_a)_{py} = 6.27\ (\sigma^\circ+0.20\Delta\bar{\sigma}_R^+-0.48\Delta\bar{\sigma}_R^-).$$

The small $r^+$ and large negative $r^-$ are in good accord with Johnson's conclusion rather than with the conclusion from the best-fit DSP correlation.

As far as the inductive contribution is concerned, all of the characteristic features of the LSFE treatment of the benzene system are found in the pyridine system, (4). In the benzene system, a bi-linear pi-electronic free energy relationship has been shown generally to result from combined meta and para substituent effects based on the inductive contribution factor of 0.85 $(=1/1.17)$:[1,3,22–25)]

$$(\Delta pK_a)^p - 0.85(\Delta pK_a)^m = C_\pi^+\sigma_\pi^+ + C_\pi^-\sigma_\pi^-.$$

Here, the $C_\pi^+$ and $C_\pi^-$ are coefficients[27)] describing pi-electronic contributions for pi-donor and pi-acceptor substituents, respectively, and are referred to as a simple function of $\rho_\pi^+$ or $\rho_\pi^-$ parameter. As shown in Fig. 1, a good bi-linear relationship intersecting at the unsubstituted point is obtained without the aid of any inductive constants, suggesting the importance of different susceptibilities (duality) to the pi-electronic effect for pi-donor and pi-acceptor substituents in the present pyridine system. The slope for the acceptor groups is close to zero, providing evidence for the small *Pi* contribution from these groups.

The actual substituent effects on the basicities of pyridines are reasonably understood by the LSFE results, characterized by the dual pi-electronic effects. Unit positive charge in the conjugate acid of pyridine probably causes a moderately exalted pi-delocalization with para pi-donor substituents as compared with the *Pi* effect in the $\sigma_p^\circ$ constant, whereas it also causes the pi-delocalization interaction with para pi-acceptor groups to be lower than that in the $\sigma_p^\circ$ (repulsive acceptor-acceptor pi-interaction). For electrophilic reactivities in the benzene system, one could observe an exalted pi-delocalization with pi-donors, but scarcely detect such a repulsive saturation in *Pi* effect with pi-acceptor substituents. The present LSFE results for the pyridine system provide further evidence sub-

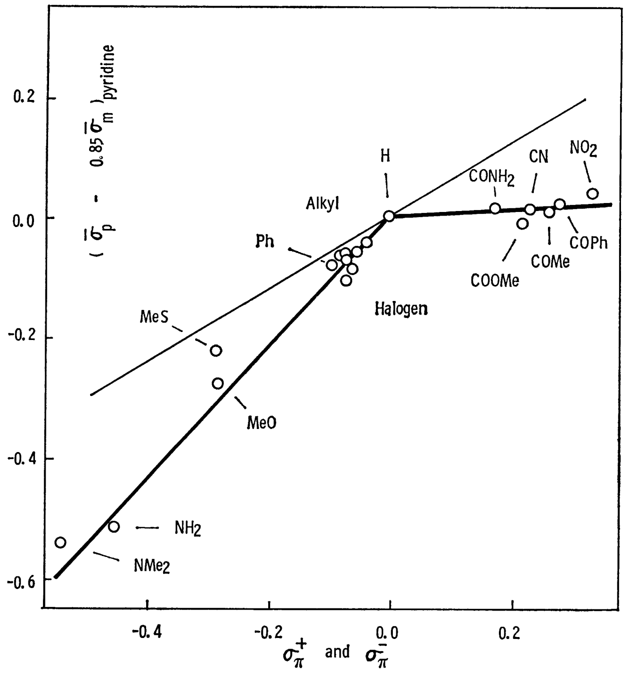

Fig. 1. The quantity of $\bar{\sigma}_p - 0.85\bar{\sigma}_m$ in the pyridine basicity against $\sigma_\pi^+$ and $\sigma_\pi^-$.
A thin line represents the corresponding plot of $\sigma_p^\circ - 0.85\sigma_m$ *vs.* $\sigma_\pi^\pm$.

stantiating the dual *Pi* effects for the analysis of substituent effects on general reactivities.

The DSP treatment,[4,8)] using one of the four distinct resonance substituent constants, also results in good correlations of comparable precision for meta and para series by means of $\sigma_R^\circ$ and $\sigma_R^+$ constants, respectively (Table 4). However, significantly different inductive effects were obtained for meta and para derivatives; $\rho_I^m = 6.40$, $\rho_I^p = 5.28$ (Table 4). From the comparison with $\rho_m$ value, the $\rho_I$ value for the meta correlation appears to be more reasonable. The higher ratio, $\rho_I^m/\rho_I^p = 1.2$, may indicate a breakdown of the original Taft assumption,[4a,e)] $\rho_I^m = \rho_I^p$. It is interesting to note that the $\rho_I$ in Johnson's correlation is nearly equal to the $\rho_I$ derived from the DSP treatment with $\sigma_R$ resonance constant (Table 4).

The LSFE treatment essentially stands on the concept that there exists a universal set of pi-electronic effect constants, $\sigma_\pi^+$ and $\sigma_\pi^-$, and that the pi-electronic contributions are expressed as a linear (or bilinear) function of $\sigma_\pi$ using dual susceptibilities of $\rho_\pi^+$ and $\rho_\pi^-$ for pi-donor and pi-acceptor substituents, respectively. The relative importance of the pi-electronic contribution from pi-acceptor/pi-donor substituents in any given system is generally accounted for by the ratio of both $\rho_\pi$ values, whereas in the DSP treatment with a single $\rho_R$ parameter, the relative importance of pi-donor/pi-acceptor resonance must be judged only by the best-fitting $\bar{\sigma}_R$ set. Continuous spectrum of $\rho_\pi^+/\rho_\pi^-$ ratio with reaction systems must be characterized by four specific $\bar{\sigma}_R$ classes in the DSP treatment. This duality for the pi-electronic contributions is the most important feature of the LSFE treatment. Johnson's treatment is an extreme case of the dual $\rho_\pi$ treatment, that is $\rho_\pi^-/\rho_\pi^+ \rightarrow 0$. The requirement for the $\sigma_R^+$ set for the best-fit DSP correlation of the present system is due simply to the high ratio of pi-donor/pi-acceptor resonance contributions; *i.e.*, $\rho_\pi^+/\rho_\pi^- = 4$.

Even though the requirement for the $\sigma_R^+$ set might imply the enhancement of pi-donor relative to pi-acceptor resonance, the enhancement of resonance relative to inductive effect is found to be quite low; $\rho_R/\rho_I \simeq 0.5$ in the pyridine para series (DSP, Table 4). Accordingly, the actual resonance contribution in this system is not so large as $\sigma_R^+$ in the $\sigma_p^+$, but is comparable with $\sigma_R$ in the $\sigma_p$ constant (since $\sigma_R^+ \simeq 1.9\sigma_R$ roughly holds for pi-donors) and the *Pi* contribution of pi-acceptors is as low as that involved in the $\sigma_m$ constant. Thus, the actual resonance effect evaluated by the best-fit DSP correlation with $\sigma_R^+$ is in fact at least qualitatively identical to that evaluated by Johnson's treatment as well as ours. Further, it is worthy of note that the $\sigma_R^+$ correlation gives excellent results with precision comparable to ours (Table 4). Johnson argued that the resonance contribution from para pi-acceptors is unreasonable, based on the observed insensitivity to steric twisting of the para nitro derivative. However, the minor resonance contribution of para pi-acceptors, comparable to that from the meta series suggested by DSP analysis, does not appear to be unreasonable, since not all the *Pi* contribution may be eliminated by means of steric twisting of the substituent. Likewise in the LSFE treatment, the *Pi* contribution estimated by the $\rho_\pi\sigma_\pi$ term should not all be referred to as the pi-delocalization effect, but may involve appreciable *I*-$\pi$ interaction, which is insensitive to the loss of coplanarity.

The point of controversy between Johnson and Taft and coworkers arises from their interpretation of the correlation results. The difference is due essentially to the basic tenet of the DSP approximation.

General reactivities are classified into four distinctly different classes, $\sigma^\circ$, $\sigma$, $\sigma^+$, and $\sigma^-$, depending on the mode of resonance interactions. The DSP treatment assumes that each class of substituent effects should be described only by a particularly suited one of four sets of resonance substituent constants, $\sigma_R^\circ$, $\sigma_R$, $\sigma_R^+$, and $\sigma_R^-$, characteristic of the corresponding reactivity classes.[4a)] In the present case, the requirement of $\sigma_R^+$ for the best-fit leads to the conclusion that the system belongs to the $\sigma^+$-class reactivity. The Johnson's $\sigma_R$-correlation, then, had to be a matter of controversy, since he also adheres to this traditional tenet. The above LSFE analysis provides a key to the solution of the controversy. Brownlee and Topsom put too much importance on the requirement of the $\sigma_R^+$ set in their interpretation,[5b)] whereas the LSFE results put importance rather more on the resulting $\lambda(=\rho_R/\rho_I)$ value in the DSP treatment, in line with Johnson's criticism. The best-fit $\bar{\sigma}_R$ does not unequivocally indicate the class of resonance demand of the system.

A closely related system, the basicities of pyridine *N*-oxides, is an instructive example in this connection. The substituent effect on the basicities was proposed to be roughly treated with the $\sigma^+$ constants for pi-donor substituents and the $\sigma^-$ constants for pi-acceptor ones.[28] For this reactivity set, the DSP treatment has been found to give excellent best-fit correlations with either the $\sigma_R$ or the $\sigma_R^+$ set.[29] Thus, the classification based on the best-fit $\bar{\sigma}_R$ set does not have any significance in this system. Further, the Johnson's treatment by no means applies to this system.

Finally, the $\Delta pK_a$ data of quinuclidines[7] can be directly incorporated into the regression analysis as an inductive measure instead of using $\sigma_i$ constants.[30]

$$(\Delta pK_a)^p_{py} = 0.93\ (\Delta pK_a)_{qu} + 9.7\sigma^+_\pi + 2.4\sigma^-_\pi \qquad (6)$$

$$(\Delta pK_a)^m_{py} = 1.12\ (\Delta pK_a)_{qu} + 3.9\sigma^+_\pi + 2.1\sigma^-_\pi \qquad (7)$$

The result again verifies our basic assumption of the duality of *Pi* contributions and the unique position dependency of the *I* contribution, $I_m/I_p = 1.17$. The effective scale of the *I* effect relative to that of quinuclidine is found to be 0.93 for the para series. This value differs appreciably from either 1.00 assumed by Taft (Eq. 2) or 1.19 employed by Johnson (Eq. 3). The problem is associated with the scaling of the inductive effects between the aromatic and the equivalent saturated systems, which will be discussed in a separate paper.

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26) According to our LSFE analysis,

$\sigma^\circ_p = 1.00\sigma_i + 1.00\sigma^+_\pi + 1.00\sigma^-_\pi$
$\sigma_p = 1.00\sigma_i + 1.65\sigma^+_\pi + 1.00\sigma^-_\pi$
$\sigma^+_p = 1.00\sigma_i + 3.41\sigma^+_\pi + 1.00\sigma^-_\pi$
$\sigma^-_p = 1.00\sigma_i + 1.00\sigma^+_\pi + 2.37\sigma^-_\pi$
$\sigma_m = 1.17\sigma_i + 0.50\sigma^+_\pi + 0.50\sigma^-_\pi$

27) The $C^+_\pi$ corresponds to the quantity of $(\rho^+_\pi)_p - 0.85(\rho^+_\pi)_m$ and the $C^-_\pi$ to $(\rho^-_\pi)_p - 0.85(\rho^-_\pi)_m$. Further, since $(\rho^+_\pi)_m = (\rho^-_\pi)_m = 0.50(\rho_i)_p$, then $C^+_\pi = (\rho^+_\pi)_p - 0.43(\rho_i)_p$ and $C^-_\pi = (\rho^-_\pi)_p - 0.43(\rho_i)_p$.

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30) For the para series, $R$=0.9974, $s$=±0.170, $n$=13. For the meta series, $R$=0.9962, $s$=±0.152, $n$=13.