

## Substituent Effects on the Reactivity of the Pyridines<sup>1,2</sup>

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The relative dissociation constants of 4-substituted bicyclo[2,2,2]octane-1-carboxylic acids, 4-substituted quinuclidines, and 3- and 4-substituted pyridines were collected from a number of sources. In order to understand the actual substituent effects with a combination of inductive effect ( $\sigma_I$ ) and resonance effect ( $\sigma_R$ ) components. The DSP correlation has been employed statistically for each of the *p*- and *m*- series. The inductive effect from the *m*- position was 1.2 times more effective than that from the *p*- position and the requirement of  $\sigma_R^+$  for the best-fit led to the conclusion that pyridine system belongs to the  $\sigma^+$ -class reactivity. Also compared with results from Yukawa-Tsuno's LArSR treatment and relevant treatment.

### Introduction

It has long been recognized that the electronic effect of a substituent depends to a certain extent upon the electron demand in the system to which it is attached. Hammett equation has been handled by defining different  $\sigma$  constant scales for systems with different electron demand (e.g.,  $\sigma$ ,  $\sigma^o$ ,  $\sigma^+$ ,  $\sigma^-$ , etc). An alternative approach to substituent effects is to divide the inductive and resonance contributions, that is, to use a Dual Substitution Parameter (DSP) approach. This approach is proposed for the approximately quantitative evaluation of resonance and inductive contributions to the effects of uncharged *m*- and *p*- substituents on the reactivities<sup>3</sup> of reaction center. And it is based on the demonstration that the scale of the inductive contributions to aromatic series reactivities is, to a good approximation, equal to that for reactivities in the aliphatic series.

The resonance contributions to aromatic series reactivities are reported, their similarity and contrasts noted, and the results are interpreted in accord with, and are shown to provide evidence for, principles from resonance theory.<sup>4</sup> Also the analysis of substituent effects in the extended  $\pi^-$  electron system of naphthalene has been discussed successively.<sup>5</sup> The same treatment should be applicable to reactivities in heteroaromatic  $\pi^-$  electron systems. Especially, *p*- and *m*-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.<sup>6</sup> 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 well handled by DSP treatment<sup>7</sup> and Tsuno and coworkers also well adjusted to the analysis of substituent effect on the basicity of pyridines by LSFE (Linear Substituent Free Energy) treatment.<sup>8</sup> But we will focus the analysis of substituent effect for pyridine system by DSP treatment.

### Results and Discussions

Hammett  $\sigma$  values are expressed by the combination of  $\sigma_I$  (Inductive Effect) and  $\sigma_R$  (Resonance Effect), i.e.,

$$\sigma = \sigma_I + \sigma_R \quad (1)$$

If  $\sigma_I$  and  $\sigma_R$  components of  $\sigma$  could be assigned to each substituent, the components would not only their interaction mechanisms be clarified but also the importance of the two effects in stabilizing the transition state could be assessed by the relative values of  $\sigma_I$  and  $\sigma_R$ . Therefore a rate series would be fitted to a two-parameter equation such as Eq. (2)

$$\log k_X/k_H = \rho_I \sigma_I + \rho_R \sigma_R \quad (2)$$

The Hammett system permits a mixture of resonance and inductive interaction to be transmitted in a given reaction series.<sup>4</sup> The ratio of  $\sigma_R$  values for the *m*- relative to that of the corresponding *p*- substituent is a constant,  $\alpha$ .

$$\sigma_p = \sigma_I + \sigma_R \quad (3)$$

$$\sigma_m = \sigma_I + \alpha \sigma_R \quad (4)$$

The factor,  $\alpha$ , may be considered a resonance effect fall-off factor between the *p*- and *m*- positions. Taft and Lewis have suggested that very generally  $\alpha \approx 0.33$ . During the reaction process, however, a strong conjugation occurs between *p*- substituent and reaction center, the  $\alpha$  value is decreased  $\sim 0.10$ .<sup>9</sup>

Some sets of reliable  $\Delta pK_a$  values of 4-substituted bicyclo[2,2,2]octane-1-carboxylic acids (I), 4-substituted quinuclidines (II), and 3- and 4-substituted pyridines (III and IV) have been collected from various sources in Table 1.<sup>10-14</sup> Each  $pK_a$  values were defined by  $pK_{H-} - pK_X$ , where their data were determined by the same authors and under the same experimental conditions respectively, unless otherwise noted. Figure 1 and Figure 2 show plots of  $\Delta pK_a(I)$  vs.  $\sigma_I$  and  $\Delta pK_a(II)$  vs.  $\sigma_I$  respectively. These are of sufficient precision in linearity to directly the validity of  $\sigma_I$  parameters because the structures of (I) and (II) have minimal resonance effect and have rigid geometry.<sup>15</sup> The plot of  $\Delta pK_a$  for the pyridines vs. Hammett  $\sigma$  values has two distinct straight-line with  $\sigma_m$  and  $\sigma_p$  values, respectively (Figure 3) and the results are

Table 1. Data of  $\Delta pK_a$ <sup>a</sup>

Subs.	I(4- $\gamma$ )	II(4- $\gamma$ )	III(3- $\gamma$ )	III(4- $\gamma$ )
NMe <sub>2</sub>	—	0.85	-1.16	-4.36
NH <sub>2</sub>	—	0.86	-0.83	-3.91
CO <sub>2</sub> <sup>-</sup>	-0.10 <sup>11</sup>	—	—	—
OMe	0.47	1.65	0.43	-1.37
OH	0.37	1.69 <sup>14</sup>	(0.4)	—
<i>t</i> -Bu	—	-0.11	-0.65	-0.82
<i>i</i> -Pr	—	-0.06	-0.55	-0.85
Et	-0.02	0.01	-0.53	-0.85
Me	-0.02	0.08	-0.46	-0.82
CH <sub>2</sub> OH	0.07	0.62 <sup>14</sup>	—	—
CH=CH <sub>2</sub>	—	0.26	—	—
CH <sub>2</sub> Cl	—	0.77	—	—
Ph	—	0.76	(0.4)	-0.14
Cl	0.77	2.34	2.40	1.38
Br	0.76 <sup>12</sup>	2.47	2.36	1.46
I	—	2.26	1.92	(1.2)
NHCOMe	—	1.42	0.77	-0.64
CO <sub>2</sub> Et	0.47	1.47 <sup>14</sup>	—	—
CO <sub>2</sub> Me	—	1.50	2.12	1.72
CO <sub>2</sub> H	0.50	—	—	—
COMe	—	1.51	1.95	1.70
OCOMe	—	2.09 <sup>14</sup>	—	—
CN	0.97 <sup>12</sup>	2.99 <sup>14</sup>	3.86	3.35
NO <sub>2</sub>	1.05	3.31	4.42	3.98
NH <sub>3</sub> <sup>+</sup>	1.23 <sup>11</sup>	—	—	—
NMe <sub>3</sub> <sup>+</sup>	1.47 <sup>11</sup>	—	—	—

<sup>a</sup>  $\Delta pK_a = pK_{aH} - pK_{aX}$ , value in brackets is chosen as the best selected values. <sup>b</sup> reference 10; <sup>c</sup> reference 13; <sup>d</sup> reference 5.

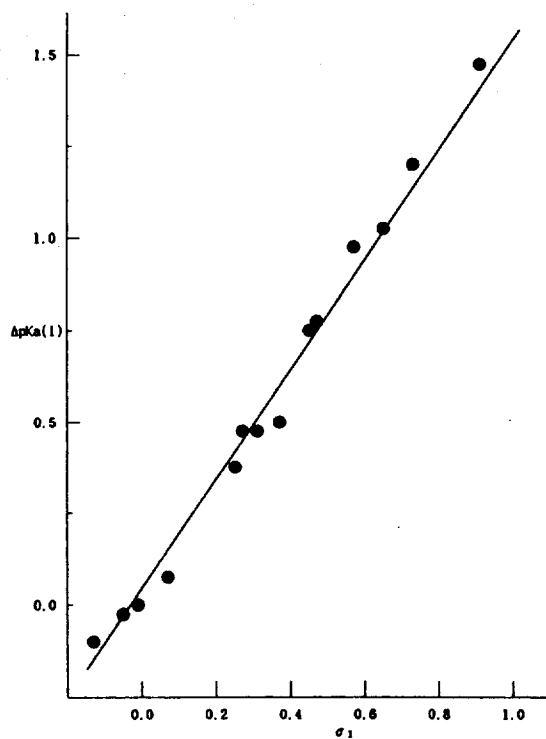


Figure 1. Plot between  $\Delta pK_a(I)$  and  $\sigma_1$   $\Delta pK_a(I) = 1.57\sigma_1 + 0.0261$  ( $R = 0.994$ ,  $SD = 0.047$ ).

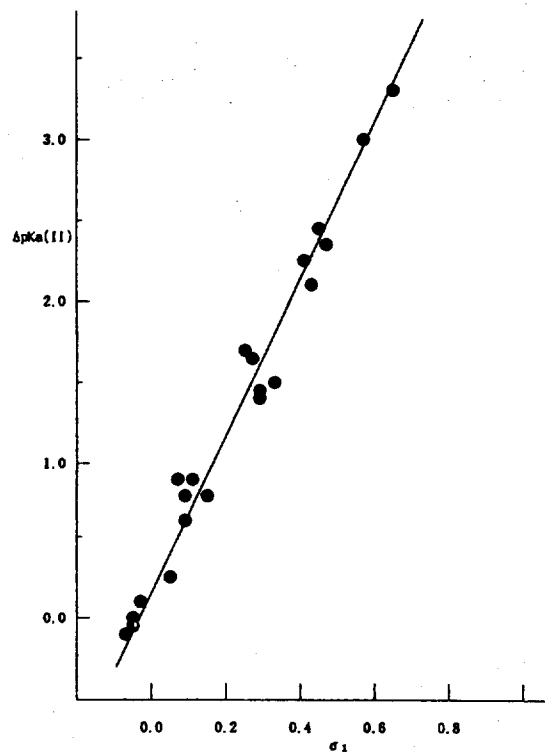


Figure 2. Plot between  $\Delta pK_a(II)$  vs.  $\sigma_1$   $\Delta pK_a(II) = 4.72\sigma_1 + 0.232$  ( $R = 0.988$ ,  $SD = 0.184$ ).

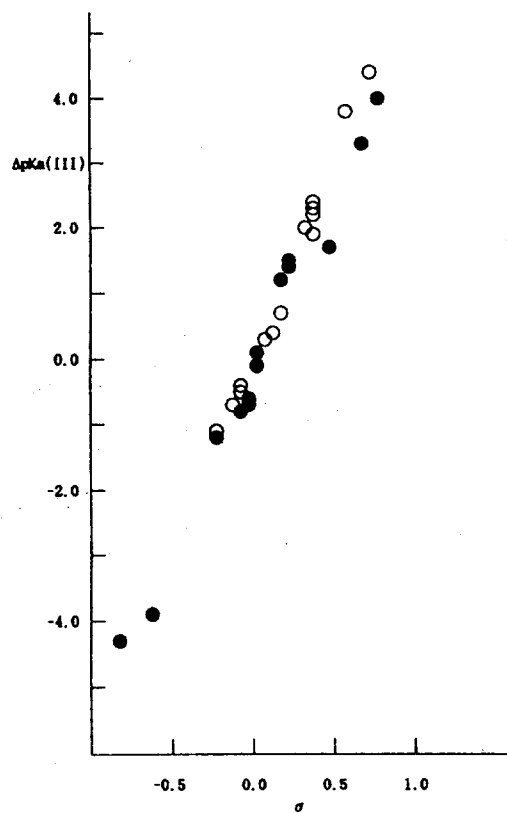
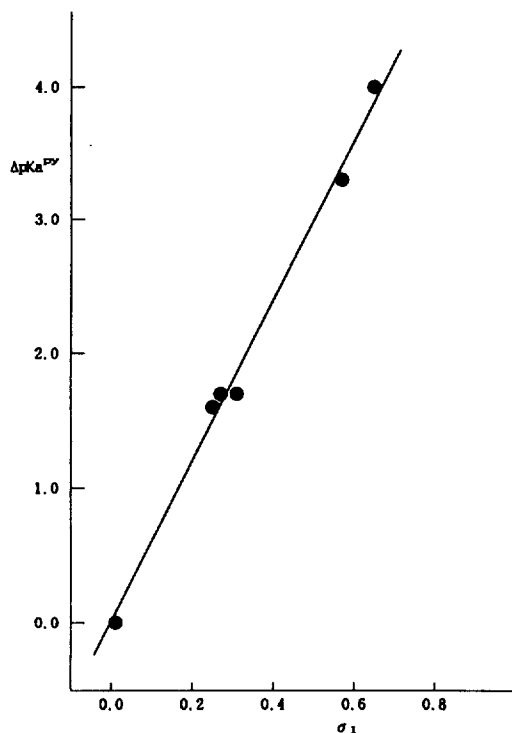


Figure 3. Plot between  $\Delta pK_a(III)$  and  $\sigma$  (●; 4-sub.pyridine, ○; 3-sub.pyridine).



**Figure 4.** Plot between  $\Delta pK_{a_{py}}$  and  $\sigma_I$  (Y-pyridine; Y=H, 4-COMe, 4-CO<sub>2</sub>Me, 4-CO<sub>2</sub>Et, 4-CN, 4-NO<sub>2</sub>).  $\Delta pK_{a_{py}} = 6.10\sigma_I - 0.0845$  ( $R = 0.995$ ,  $SD = 0.350$ ).

Eq. (5) and (6).

$$\Delta pK_{a_{py}}^p = 5.06 \sigma_p - 0.137 \quad (R = 0.991, SD = 0.166) \quad (5)$$

$$\Delta pK_{a_{py}}^m = 6.16 \sigma_m - 0.056 \quad (R = 0.992, SD = 0.183) \quad (6)$$

Figure 4 shows the plot of  $\Delta pK_a$  for the dipolar electron-withdrawing groups (CO<sub>2</sub>Me, CO<sub>2</sub>Et, COMe, CN, NO<sub>2</sub>) of pyridine vs.  $\sigma_I$  values. This slope is well fitted with single-line and the result is given in Eq. (7).

$$\Delta pK_{a_{py}} = 6.10 \sigma_I - 0.0845 \quad (R = 0.995, SD = 0.350) \quad (7)$$

These electron-withdrawing substituents appear to be exerting the inductive effect only. It seems reasonable to expect that the dipolar electron-withdrawing groups will be far more difficult to withdraw electron density from the nitrogen nucleus of pyridine than from the reacting atom of the benzene moiety.<sup>16</sup> The result of a least squares calculation agrees well with  $\rho_m$  (Eq. (6)).

Based on Eq. (7),  $\sigma_{py}$  values for the pyridine system are evaluated from  $\Delta pK_a$  of pyridines and these results are listed in Table 2. Table 3 enlists some results of application.

The value of  $\Delta pK_{a_{py}} - \Delta pK_{a_{4-qu}}$  should be a resonance factor ( $\sigma_R$ ), because the structure of 4-substituted quinuclidines includes only inductive factor ( $\sigma_I$ ) and their structure is similar to pyridine which oriented by  $\sigma_I$  and  $\sigma_R$  factors. Among the plots between  $\log(K/K_o)_{4-py} - \log(K/K_o)_{4-qu}$  (except substituent with CO<sub>2</sub>Me-, CO<sub>2</sub>Et-, COMe-, CN-, and NO<sub>2</sub>-) and resonance factors ( $\sigma_R^0$ ,  $\sigma_R(\text{BA})$ , and  $\sigma_R^+$ ), the plot with  $\sigma_R^+$  is quite well correlated with linearity (eq. (8), (9), (10)).

$$\log(K/K_o)_{4-py} - \log(K/K_o)_{4-qu} = 7.96\sigma_R^0 - 0.180 \quad (R = 0.920, SD = 1.02) \quad (8)$$

$$\log(K/K_o)_{4-py} - \log(K/K_o)_{4-qu} = 5.21\sigma_R(\text{BA}) - 0.340 \quad (R = 0.972, SD = 0.382) \quad (9)$$

$$\log(K/K_o)_{4-py} - \log(K/K_o)_{4-qu} = 2.84\sigma_R^+ - 0.111 \quad (R = 0.994, SD = 0.0972) \quad (10)$$

**Table 2.** Apparent  $\sigma$  and Related  $\sigma$  Values for LFER

$\sigma$	$\sigma$		$\sigma_{py}^a$		$\sigma_I^b$	$\sigma_R^{0b}$	$\sigma_R(\text{BA})^b$	$\sigma_R^{+b}$
	<i>m</i> -	<i>p</i> -	<i>m</i> -	<i>p</i> -				
NMe <sub>2</sub>	-0.21	-0.83	-0.171	-0.690	0.06	-0.52	-0.83	-1.75
NH <sub>2</sub>	-0.15	-0.66	-0.117	-0.617	0.12	-0.48	-0.82	-1.61
OMe	0.115	-0.27	0.087	-0.205	0.27	-0.45	-0.61	-1.02
OH	0.12	-	0.08	-	0.25	-0.43	-	-
<i>t</i> -Bu	-0.10	-0.20	-0.088	-0.116	-0.07	-	-	-0.18
<i>i</i> -Pr	-0.07	-0.156	-0.072	-0.121	-0.06	-	-	-0.21
Et	-0.07	-0.15	-0.069	-0.121	-0.05	-	-	-0.23
Me	-0.069	-0.17	-0.057	-0.116	-0.04	-0.11	-0.11	-0.25
Ph	-	0.039	0.08	-0.005	0.10	-0.11	-0.11	-0.30
Cl	0.373	0.23	0.407	0.241	0.46	-0.23	-0.23	-0.36
Br	0.391	0.23	0.400	0.254	0.44	-0.19	-0.19	-0.30
I	0.352	0.28	0.329	0.21	0.39	-0.16	-0.16	-0.15
NHCOMe	0.12	0.00	0.14	-0.086	0.26	-0.25	-0.36	-0.86
CO <sub>2</sub> Et	0.36	0.47	0.36	0.30	0.30	0.14	0.14	0.14
CO <sub>2</sub> Me	0.36	0.46	0.361	0.296	0.34	0.14	0.14	0.14
COMe	0.376	0.491	0.334	0.293	0.28	0.16	0.16	0.16
CN	0.56	0.653	0.643	0.561	0.56	0.13	0.13	0.13
NO <sub>2</sub>	0.71	0.78	0.734	0.663	0.65	0.15	0.15	0.15

<sup>a</sup> $\sigma_{py}$ 's are evaluated from  $\Delta pK_a$  of pyridines ( $\sigma = 0.162 \Delta pK_a + 0.0173$ ). <sup>b</sup>Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*; Harper & Row, Publishers; New York, U.S.A., 1982; Chap. 2 and reference 7. a).

Table 3. Some Applications of  $\sigma_{py}$  and  $\sigma$  Values

Reaction	solvent	temp.(°C)	$\rho_{py}^a$	$R^b$	SD <sup>c</sup>	$\rho$	R	SD	Rxn.no.	ref.
<i>p</i> -CH <sub>3</sub> O-C <sub>6</sub> H <sub>4</sub> OSO <sub>2</sub> Cl + NC <sub>5</sub> H <sub>4</sub> -(Y)→ <i>p</i> -CH <sub>3</sub> O-C <sub>6</sub> H <sub>4</sub> OSO <sub>2</sub> N <sup>+</sup> C <sub>5</sub> H <sub>4</sub> -(Y) Cl <sup>-</sup>	water	25	-2.48	0.999	0.042	-2.26	0.984	0.184	8	18
<i>p</i> -CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub> OSO <sub>2</sub> Cl + NC <sub>5</sub> H <sub>4</sub> -(Y)→ <i>p</i> -CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub> OSO <sub>2</sub> N <sup>+</sup> C <sub>5</sub> H <sub>4</sub> -(Y) Cl <sup>-</sup>	water	25	-2.69	0.999	0.051	-2.56	0.984	0.198	8	18
C <sub>6</sub> H <sub>5</sub> OSO <sub>2</sub> Cl + NC <sub>5</sub> H <sub>4</sub> -(Y)→ C <sub>6</sub> H <sub>5</sub> OSO <sub>2</sub> N <sup>+</sup> C <sub>5</sub> H <sub>4</sub> -(Y) Cl <sup>-</sup>	water	25	-2.78	0.999	0.046	-2.55	0.984	0.204	8	18
<i>m</i> -NO <sub>2</sub> -C <sub>6</sub> H <sub>5</sub> OSO <sub>2</sub> Cl + NC <sub>5</sub> H <sub>4</sub> -(Y)→ <i>m</i> -NO <sub>2</sub> -C <sub>6</sub> H <sub>5</sub> OSO <sub>2</sub> N <sup>+</sup> C <sub>5</sub> H <sub>4</sub> -(Y) Cl <sup>-</sup>	water	25	-3.32	0.999	0.039	-3.04	0.986	0.233	8	18
<i>p</i> -NO <sub>2</sub> -C <sub>6</sub> H <sub>5</sub> OSO <sub>2</sub> Cl + NC <sub>5</sub> H <sub>4</sub> -(Y)→ <i>p</i> -NO <sub>2</sub> -C <sub>6</sub> H <sub>5</sub> OSO <sub>2</sub> N <sup>+</sup> C <sub>5</sub> H <sub>4</sub> -(Y) Cl <sup>-</sup>	water	25	-3.39	0.999	0.045	-3.11	0.986	0.231	8	18
<i>p</i> -CH <sub>3</sub> O-C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CH <sub>2</sub> -ONs + NC <sub>5</sub> H <sub>4</sub> -(Y)→ <i>p</i> -CH <sub>3</sub> O-C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CH <sub>2</sub> N <sup>+</sup> C <sub>5</sub> H <sub>4</sub> -(Y) <sup>-</sup> ONs	MeCN	70	-1.59	0.992	0.115	-1.43	0.989	0.125	5	19
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CH <sub>2</sub> OSO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> - <i>p</i> -CH <sub>3</sub> + NC <sub>5</sub> H <sub>4</sub> -(Y)→ C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CH <sub>2</sub> N <sup>+</sup> C <sub>5</sub> H <sub>4</sub> -(Y) <sup>-</sup> OSO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> - <i>p</i> -CH <sub>3</sub>	MeCN	70	-1.31	0.991	0.0739	-1.28	0.987	0.0858	9	20
C <sub>6</sub> H <sub>5</sub> COCH <sub>2</sub> Br + NC <sub>5</sub> H <sub>4</sub> -(Y)→ C <sub>6</sub> H <sub>5</sub> COCH <sub>2</sub> N <sup>+</sup> C <sub>5</sub> H <sub>4</sub> -(Y) Br <sup>-</sup>	MeOH	45	-1.76	0.992	0.086	-1.70	0.98	0.130	9	21
<i>p</i> -Cl-C <sub>6</sub> H <sub>5</sub> COCH <sub>2</sub> Br + NC <sub>5</sub> H <sub>4</sub> -(Y)→ <i>p</i> -ClC <sub>6</sub> H <sub>5</sub> COCH <sub>2</sub> N <sup>+</sup> C <sub>5</sub> H <sub>4</sub> -(Y) Br <sup>-</sup>	MeOH	45	-1.86	0.990	0.098	-1.79	0.973	0.160	9	21
<i>p</i> -CH <sub>3</sub> O-C <sub>6</sub> H <sub>5</sub> COBr + NC <sub>5</sub> H <sub>4</sub> -(Y)→ <i>p</i> -CH <sub>3</sub> O-C <sub>6</sub> H <sub>5</sub> CON <sup>+</sup> C <sub>5</sub> H <sub>4</sub> -(Y) Br <sup>-</sup>	MeOH	45	-1.83	0.988	0.111	-1.77	0.971	0.164	9	21
CH <sub>3</sub> OSO <sub>2</sub> F + NC <sub>5</sub> H <sub>4</sub> -(Y)→ CH <sub>3</sub> OSO <sub>2</sub> N <sup>+</sup> C <sub>5</sub> H <sub>4</sub> -(Y) F <sup>-</sup>	2-nitro-propane	25	-2.66	0.999	0.0434	-2.51	0.986	0.188	7	22
C <sub>2</sub> H <sub>5</sub> OSO <sub>2</sub> F + NC <sub>5</sub> H <sub>4</sub> -(Y)→ C <sub>2</sub> H <sub>5</sub> OSO <sub>2</sub> N <sup>+</sup> C <sub>5</sub> H <sub>4</sub> -(Y) F <sup>-</sup>	2-nitro-propane	25	-2.11	0.997	0.078	-1.99	0.980	0.178	7	22
<i>p</i> -Me-C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> OSO <sub>2</sub> C <sub>6</sub> H <sub>5</sub> + NC <sub>5</sub> H <sub>4</sub> -(Y)→ <i>p</i> -MeC <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> N <sup>+</sup> C <sub>5</sub> H <sub>4</sub> -(Y) <sup>-</sup> OSO <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	MeCN	35	-1.85	0.994	0.085	-1.89	0.988	0.119	8	23
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> OSO <sub>2</sub> C <sub>6</sub> H <sub>5</sub> + NC <sub>5</sub> H <sub>4</sub> -(Y)→ C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> N <sup>+</sup> C <sub>5</sub> H <sub>4</sub> -(Y) <sup>-</sup> OSO <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	MeCN	35	-2.04	0.997	0.0674	-2.08	0.991	0.112	8	23
<i>m</i> -Br-C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> OSO <sub>2</sub> C <sub>6</sub> H <sub>5</sub> + NC <sub>5</sub> H <sub>4</sub> -(Y)→ <i>m</i> -Br-C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> N <sup>+</sup> C <sub>5</sub> H <sub>4</sub> -(Y) <sup>-</sup> OSO <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	MeCN	35	-2.16	0.998	0.0566	-2.21	0.994	0.101	8	23
<i>p</i> -NO <sub>2</sub> -C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> OSO <sub>2</sub> C <sub>6</sub> H <sub>5</sub> + NC <sub>5</sub> H <sub>4</sub> -(Y)→ <i>p</i> -NO <sub>2</sub> -C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> N <sup>+</sup> C <sub>5</sub> H <sub>4</sub> -(Y) <sup>-</sup> OSO <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	MeCN	35	-2.44	0.997	0.0873	-2.48	0.991	0.134	8	23

<sup>a</sup> results of Hammett plot with  $\sigma_{py}$ . <sup>b</sup> correlation coefficient. <sup>c</sup> standard deviation.

Table 4. Reactions correlated by Dual Substitution Parameters<sup>a</sup>

Reaction	$\rho_I^{meta}$	$\rho_R^{meta}$	$\lambda_{meta}^b$	$\rho_I^{para}$	$\rho_R^{para}$	$\lambda_{para}$
A. With the $\sigma_R(BA)$ scale						
ArCO <sub>2</sub> H, ioniz., H <sub>2</sub> O, 25°C	1.00	0.28	0.28	1.00	1.00	1.01
Ioniz., 43.5% aq-dioxane, 25°C	1.34	0.62	0.46	1.43	1.15	0.81
Ion-pair form., 1,3-DPG, benzene, 25°C	2.15	0.70	0.33	1.98	1.36	0.69
Ioniz., gas phase	9.8	3.53	0.36	10.80	5.08	0.47
B. With the $\sigma_R^+$ scale						
ArCMe <sub>2</sub> Cl, solv., 90% aq-H <sub>2</sub> SO <sub>4</sub> , 25°C				-4.639	-4.657	1.00
ArC(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> OH, ioniz., aq-H <sub>2</sub> SO <sub>4</sub> , 25°C				-4.521	-5.557	1.23
Ar <sub>2</sub> C(C <sub>6</sub> H <sub>5</sub> )OH, ioniz., aq-H <sub>2</sub> SO <sub>4</sub> , 25°C				-8.085	-7.895	0.98
Ar <sub>3</sub> COH, ioniz., aq-H <sub>2</sub> SO <sub>4</sub> , 25°C				-11.10	-9.793	0.88
PyrH <sup>+</sup> , ioniz., H <sub>2</sub> O, 25°C <sup>c</sup>	6.21	1.03	0.17	5.17	2.68	0.52
PyrH <sup>+</sup> , ioniz., H <sub>2</sub> O, 25°C				5.28	2.71	0.51
ArN <sub>2</sub> <sup>+</sup> →ArOH, decomp., H <sub>2</sub> O, 29°C				-4.086	2.722	-0.67
ArCHO, cannizaro reaction, 50% aq-MeOH, 100°C				4.426	2.217	0.48

C. With the $\sigma_R^0$ scale						
ArCO <sub>2</sub> H, ioniz., H <sub>2</sub> O, 25°C	0.992	0.403	0.41			
ArCH <sub>2</sub> CO <sub>2</sub> H, ioniz., 50% aq-EtOH, 25°C				0.755	0.646	0.86
D. With the $\sigma_R^-$ scale						
ArNH <sub>3</sub> , ioniz., H <sub>2</sub> O, 25°C <sup>d</sup>				3.09	3.48	1.13

<sup>a</sup>ref. 15. b)  $\lambda = \rho_R/\rho_I$ . <sup>c</sup>This work. <sup>d</sup>ref. 6 a).

An application of the DSP treatment by using  $\sigma_R^+$  constants, these plots are in good correlation with *p*- and *m*-series of pyridines, respectively (Eq. (11), (12)).

$$\log(K/K_0)^p = 5.17\sigma_1 + 2.68\sigma_R^+ - 0.0282$$

$$(R=0.998, SD=0.0177) \quad (11)$$

$$\log(K/K_0)^m = 6.21\sigma_1 + 1.03\sigma_R^+ + 0.0114$$

$$(R=0.996, SD=0.0179) \quad (12)$$

Table 4 enlisted the results of the DSP analysis. However, significantly different inductive effects are obtained for the *p*- and *m*- derivatives;  $\rho_I^m = 6.21$ ,  $\rho_I^p = 5.17$ . From the comparison with Eqn. (7), the  $\rho_I$  value for the meta correlation appears to be more reasonable. The ratio,  $\rho_I^m/\rho_I^p = 1.20$ , may be indicated a breakdown of the original Taft assumption,  $\rho_I^m = \rho_I^p^{6.17}$  but this is consistent with the result of Yukawa-Tsuno's LSFE correlation for the pyridine system,  $\rho_I^m/\rho_I^p = 1.18$  and 1.17 for the benzene system.<sup>7</sup> 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 quiet low;  $\rho_R/\rho_I = 0.52$ , in *p*- series and  $\rho_R/\rho_I = 0.17$  in *m*- series of pyridines. Whereas, inductive effect for *m*- derivatives of pyridine,  $\rho_I^m$ , is found to be 6.21, which is virtually identical with Eq. (7). So,  $\rho_I$  put 6.10 and LArSR (Linear Aromatic Substituent Reactivity) treatment applies both for *p*- and *m*-series in the present system. This results were Eq. (13) and (14).

$$\log(K/K_0)^p = 6.10\sigma_1 + 2.47(\sigma_R^0 + 1.06 \Delta\sigma_R^+ - 0.112 \Delta\sigma_R^-)$$

$$(R=0.998, SD=0.0254) \quad (13)$$

$$\log(K/K_0)^m = 6.10\sigma_1 + 1.63(\sigma_R^0 + 0.631 \Delta\sigma_R^+ + 0.176 \Delta\sigma_R^-)$$

$$(R=0.998, SD=0.0194) \quad (14)$$

The result that  $\rho_I$  value is greater than  $\rho_R$  value for both *p*- and *m*- series, respectively seems a weak conjugation during the reaction process between a substituent and reacting atom. However Yukawa-Tsuno's resonance demand of  $R^+$ ,  $r_R^+$ , for *p*- series of pyridine is greater than that of *m*- series. For *p*- derivatives, the resonance interaction between substituent and positive charge produced at the reaction center is more demanded than *m*- derivatives and this is the same results of Eq. (11) and (12).

General reactivities are classified into four distinctly different class,  $\sigma^0$ ,  $\sigma(\text{BA})$ ,  $\sigma^+$ , and  $\sigma^-$ , depending on the mode of resonance interaction. 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,  $\sigma_R^0$ ,  $\sigma_R(\text{BA})$ ,  $\sigma_R^+$ , and  $\sigma_R^-$ , characteristic of the corresponding reactivity class. In the present case, the requirement of  $\sigma_R^+$  for the best-fit leads to the conclusion

that the system belongs to the  $\sigma_R^+$ -class reactivity.

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## Formation and Reactions of $\alpha$ -Phosphoryl Thiocarbocations: Synthesis of $\alpha$ -Sulfenyl Phosphonates

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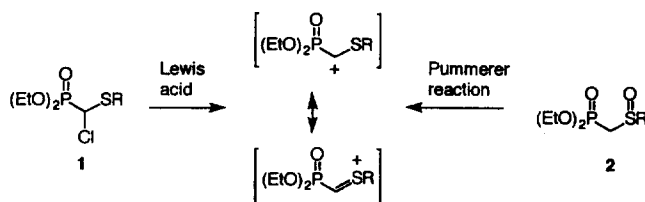
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The reaction of chloro(methylthio and arylthio)methanephosphonate (**1**) and Pummerer-type reaction of sulfinylmethanephosphonate (**2**) with nucleophiles such as aromatic compounds and thiols were examined. The direct chlorination of (methylthio and arylthio)methanephosphonate with *N*-chlorosuccinimide (NCS) led to the formation of monochlorinated phosphonates (**1**) in good yield. The reaction of **1** with aromatic compounds and thiols in the presence of stannic chloride afforded a variety of aryl(methylthio)methanephosphonates (**3**) and thioacetals of formylphosphonates (**4**), respectively. Phosphonates **3** and **4** were also obtained from the reaction of Pummerer intermediate, generated from sulfinylmethanephosphonate (**2**), with aromatic compounds and thiols, respectively. A versatile reaction conditions to generate Pummerer intermediate were examined. The best condition was the combination of trifluoroacetic anhydride with stannic chloride. All reactions may involve an initial formation of  $\alpha$ -phosphoryl thiocarbocation and a subsequent nucleophilic attack of aromatic compounds and thiols.

### Introduction

Phosphonates are important reagents for the construction of carbon-carbon double bonds because their use provides control of olefin regio- and stereoselectivity.<sup>1</sup> Phosphonates containing organic sulfur group have emerged as the subject of considerable interest in organic synthesis.<sup>2</sup> In our preliminary report we described the reaction of chloro(methylthio and arylthio)methanephosphonate (**1**)<sup>3</sup> and Pummerer-type reaction of sulfinylmethanephosphonate (**2**)<sup>4</sup> with various nucleophiles to afford several  $\alpha$ -sulfenyl substituted phosphonates. These reactions involve the generation of  $\alpha$ -phosphoryl thiocarbocations as the corresponding intermediates from either the treatment of **1** with Lewis acid or Pummerer rearrangement of **2** (Scheme 1).

According to the previous report,<sup>5</sup> aryl(methylthio)methanephosphonates (**3**) was converted into aromatic ketones under the Horner-Wadsworth-Emmons reaction conditions followed by hydrolysis. The preparation of **3** results from the addition of the elemental sulfur<sup>5</sup> or disulfide<sup>6</sup> to arylmethanephosphonate cabanion and the reaction of thioacetal with phosphite<sup>7</sup> to overcome the synthetic limitation of aryl substituent in Arbusov reaction. Thioacetals of formylphosphonate (**4**) are the precursors of ketene thioacetals which



Scheme 1.

are reagents of great synthetic potential. So far a few reports on the synthesis of **4** have been found in the literature.<sup>8</sup> In this report the syntheses of aryl(methylthio)methanephosphonates and thioacetals of formylphosphonate will be described in detail (Scheme 2).

### Results and Discussion

**Synthesis of Aryl(methylthio)methanephosphonates.** Chloro(methylthio and arylthio)methanephosphonates (**1**) were prepared from direct chlorination of methyl (and aryl)thiomethanephosphonate with *N*-chlorosuccinimide (NCS) and used for further reaction without purification (Table 1).<sup>3a</sup> Given the best yields by using a 10-20% excess