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Replacement Substituent Constants for Simple Heterocycles

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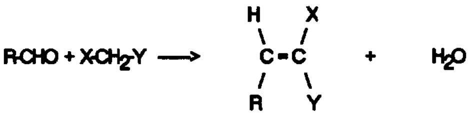
ABSTRACT

^{13}C nmr absorptions are reported for the β-vinylic carbon atoms in 15 series of ethylenes bearing heterocyclic substituents. The data are used to establish the best single-parameter substituent constants, σ^{13}, for the various heterocycles as replacements for *para*-substituted benzenes. Also reported are replacement dual substituent constants, including σ_I and the various σ_R scales needed in the Taft DSP treatment and those for F and R used in the Swain-Lupton treatment. Values of σ^{13}, F, R, σ_I, and $\sigma_R o$, respectively, for the various heterocycles as replacements for *para*-substituted benzenes are as follows: 2-furyl, -1.01, 0.99, -2.51, 0.65, -0.60; 2-pyrryl, -2.53, 0.52, -5.09, -0.16, -0.62; 2-thienyl, -0.79, 2.49, -3.60, 1.82, -1.08; 3-thienyl, -0.40, 1.04, -1.57, 0.59, -0.39; 2-pyridyl, 0.88, 2.09, -0.24, 1.65, -0.45; 3-pyridyl, 0.60, 0.57, 0.63, 0.35, 0.04; and 4-pyridyl, 1.18, 1.22, 1.09, 0.92, -0.01. The DSP-NLR method of analysis is explored using electron demand parameters, ε, as determined for the vinylic side chains in *para*-substituted styrenes.

INTRODUCTION

The effect of substituents attached to heterocycles can normally be correlated well by means of standard Hammett-type substituent constants, although it is clear that the transmission of electronic effects through heterocyclic rings is scaled differently than transmission through a benzene nucleus. Consequently, heterocyclic data must be treated independently from analogous data for substituted benzenes. Jaffe suggested in 1953 that the heteroatom in a pseudoaromatic ring can be viewed as a replacement for either a -CH=CH- or -CH= unit in a benzene ring.[2] In this way, replacement substituent constants can be defined for heterocyclic rings and such constants should permit the analysis of heterocyclic effects to be incorporated into that for substituted benzenes. Since then, a substantial amount of work has been directed toward defining Hammett-type replacement substituent constants for heterocyclic rings and many values of σ and σ^+ constants have been reported. Perhaps unfortunately, the literature, which was reviewed by Charton in 1978,[3] suggests that such constants for simple heterocycles are of limited utility because of the wide variations in the values obtained when different methods of evaluation are employed. Thus, replacement σ values determined for some of the systems surveyed by Charton have shown the following ranges: 2-furyl, 0.10 to 1.08; 2-pyrryl, -0.15 to -0.58; 2-thienyl, -0.15 to 0.71; 3-thienyl, -0.01 to 0.12; 2-pyridyl, 0.37 to 1.1; 3-pyridyl, 0.10 to 1.3; and 4-pyridyl, 0.6 to 1.6. Similarly broad ranges have been reported for σ^+ values. Because of these variations, Charton suggested that the dual substituent parameter (DSP) treatment of Taft,[4] the 2-parameter treatment of Yukawa and Tsuno,[5] his own LD treatment,[6] or other 2-parameter treatments might represent more promising pathways for handling heterocyclic data. At present, however, there is a paucity of information concerning replacement substituent constants for use in 2-parameter treatments. Tupitsyn, Zatsepina, Kolodina, and Kaminskii reported σ_I values of 0.7, 0.6, 0.9, and 0.4 for the 2-furyl, 3-furyl, and 3-thienyl groups, respectively, based on an analysis of C-H stretching frequencies in substituted furans and thiophenes.[7] Kaminskii[8] calculated values of σ_I and σ_R^o as follows (heteroaromatic group, σ_I, σ_R^o): 2-furyl, 0.53, -0.07; 3-furyl, 0.44, -0.28; 2-thienyl, 0.63, -0.03; 3-thienyl, 0.43, -0.14; 2-pyrryl, 0.22, -0.17; and 3-pyrryl, 0.22, -0.66. Similarly, Angelelli, Katritzky, Pinzelli, and Topsom analysed frequencies and intensities of various ring vibrational modes to find σ_R^o values of -0.14 and -0.13 for the thienyl and furyl groups, respectively.[9] In these latter cases, a distinction between positions of attachment could not be made.



$$RCHO + XCH_2Y \longrightarrow \begin{matrix} H & & X \\ & C=C & \\ R & & Y \end{matrix} + H_2O \qquad (1)$$

3-22

	R	Series	X	Y
a:	2-Furyl	3	CN	H
b:	2-Pyrryl	4	CN	CN
c:	2-Thienyl	6	Ph	CN
d:	3-Thienyl	7	CO_2Et	CN
e:	2-Pyridyl	8	COPh	CN
f:	3-Pyridyl	9	PO_3Et_2	CN
g:	4-Pyridyl	10	COMe	COMe
		11	COMe	CO_2Et
		12	CO_2Et	CO_2Et
		13	PO_3Et_2	CO_2Et
		14	COMe	H
		15	H	CN
		16	CO_2Et	COMe
		17	Co-*t*-Bu	H
		19	COPh	H
		20	CO_2Et	H
		22	COPh	CO_2Et

We have previously reported ^{13}C nmr data for 17 series of *meta*- and *para*-substituted styrenes and analyses of these data by application of a variety of DSP treatments, as well as an analysis utilizing the field and resonance parameters appropriate for the Swain-Lupton equation.[10,11] We have now extended many of these series to include the 2-furyl, 2-pyrryl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, and 4-pyridyl groups as replacements for the substituted benzene moieties. By utilizing the present data in conjunction with those previously reported, we are able to derive a variety of replacement substituent constants for these 7 common heterocyclic groups.

Experimental

Syntheses were effected by condensing the appropriate aldehydes with substances containing an active methylene group, as depicted in eq 1. For convenience in reference, the series numbering is the same as that previously given for *meta*- and *para*-substituted benzene analogs.[11] Condensation typically proceeded in routine fashion by the methods previously described,[10] although for some series the best solvent/catalyst combination had to be selected from a wide variety of options.[12] In a few cases, indicated by omissions in Table I, the desired reaction could not be conveniently effected. In all, 100 compounds are included in this study and 84 of these have been described in the literature. For the remaining 16, the method of synthesis and the spectral characterizations served as positive identification of structure. In all instances, the ^{13}C nmr spectra accorded completely with structure. These spectra were recorded by means of a Varian CFT-20 spectrometer. CDC1$_3$ was used as solvent and solutions typically contained 0.5 g solute in 1.5 mL. In a few cases of lower solubility, more dilute solutions were used. Chemical shifts are reported as ppm downfield from the internal reference, TMS. Peak assignments were made from coupled and decoupled spectra on the basis of shifts and relative peak heights in the spectra of known compounds. In some cases, off-resonance decoupled spectra were also useful. The chemical shift of the vinylic carbon atom β to the heteroaromatic ring in each compound studied is given in Table I.

Results and Discussion

σ^{13} Constants. The best set of single replacement substituent constants for the heterocycles can be calculated in the same manner employed for the *meta*- and *para*-substituted benzene series previously reported.[10,11] This method utilizes eq 2, for which the *a* value is defined in eq 3. In this latter equation, σ^{13} for the *p*-NMe$_2$ substituent was arbitarily set at -1.75 to scale the values to the σ^+ scale. This led to σ^{13} constants that were very close to σ^+

Table I. ^{13}C chemical shifts for vinylic β-carbon atoms.[a]

	Heteroaromatic Substituent						
Series	2-Furyl	2-Pyrryl	2-Thienyl	3-Thienyl	2-Pyridyl	3-Pyridyl	4-Pyridyl
3	93.23	-	94.44	95.45	-	98.88	101.5
4	77.31	70.01	75.92	80.53	-	85.44	88.50
6	107.54	101.44	108.30	109.73	114.86	114.23	116.64
7	98.73	91.93	99.42	101.37	106.88	105.88	108.40
8	105.41	99.07	106.16	108.19	-	-	-
9	95.26	85.59	-	97.92	-	-	-
10	138.34	135.92	139.10	140.73	144.50	144.84	146.06
11	130.28	121.43	130.47	132.74	136.55	136.44	138.25
12	122.25	113.81	122.60	124.41	129.23	129.08	130.66
13	-	-	-	121.77	-	-	-
14	124.34	120.79	125.69	126.96	130.29	128.84	130.76
15	91.18	-	91.79	93.14	-	97.89	100.38
16	129.82	119.88	129.54	132.01	137.08	136.44	137.99
17	118.44	114.46	119.76	120.53	124.56	122.71	124.86
19	119.28	115.29	120.91	121.84	125.53	123.73	126.17
20	116.06	-	117.07	117.96	122.45	120.50	123.00
22	127.46	120.56	128.46[b]	129.56	134.66	134.07	136.19

[a] Spectra were recorded on CDC1$_3$ solutions typically containing 0.5 g solute in 1.5 mL. Shifts are ppm downfield from TMS as internal reference. [b] Assignment uncertain.

constants for electron-donating groups, but were intermediate between σ^+ and σ^- values for electron-withdrawing groups. The σ^{13} values calculated from each series studied with the present heterocycles are collected in Table II. As seen, the σ^{13} values obtained for each heterocycle in the various series show reasonable agreement among themselves, although

$$\sigma_X^{13} = a\,(\delta_X - \delta_H) \qquad (2)$$

$$-1.75 = a\,(\delta_{p\text{-NMe2}} - \delta_H) \qquad (3)$$

there are a few notable exceptions, particularly in the case of the 2-pyrryl group. According to the σ^{13} values found, the 2-pyrryl group is the strongest electron donor. Replacement of a benzene ring by a 2-pyrryl group provides greater electron donation than does the substitution of a *p*-dimethylamino group (σ^+ = -1.7) for the *p*-hydrogen atom. Similarly, replacement by the 2-furyl group provides greater electron donation than does the presence of a *p*-methoxy group (σ^+= -0.78). Replacement by the 2- and 3-thienyl groups are approximately equivalent to the presence of *p*-methoxy and *p*-methyl (σ^+ = -0.31) substituents, respectively. The pyridyl group is electron withdrawing in all its attachments. Replacement by 4-, 3-, and 2-pyridyl is approximately equivalent to the presence of *p*-nitro (σ^- = 1.24), *m*-cyano (σ^- = 0.56), and *p*-cyano (σ^- = 0.90) groups, respectively. To test the validity of the mean σ^{13} values thus calculated, the data for all series except 9 and 13, for which limited data are available, were analyzed by means of eq 4 and the results of

Table II. σ^{13} constants derived from eq 2.

	Heteroaromatic Substituent						
Series	2-Furyl	2-Pyrryl	2-Thienyl	3-Thienyl	2-Pyridyl	3-Pyridyl	4-Pyridyl
3	-0.80	-	-0.50	-0.24	-	0.63	1.24
4	-0.88	-2.06	-0.77	-0.36	-	0.44	0.93
6	-0.97	-2.41	-0.79	-0.46	0.75	0.61	1.18
7	-0.85	-2.16	-0.72	-0.34	0.71	0.51	1.01
8	-0.99	-2.27	-0.84	-0.43	-	-	-
9	-0.86	-2.37	-	-0.44	-	-	-
10	-1.53	-2.33	-1.28	-0.73	0.52	0.64	1.04
11	-1.37	-2.32	-1.32	-0.63	0.53	0.50	0.97
12	-1.16	-3.42	-1.07	-0.57	0.71	0.67	1.09
13	-	-	-	-0.67	-	-	-
14	-0.97	-2.23	-0.49	-0.04	1.14	0.63	1.31
15	-0.93	-	-0.79	-0.47	-	0.65	1.32
16	-1.23	-3.98	-1.31	-0.62	0.78	0.60	1.40
17	-0.86	-2.18	-0.36	-0.09	1.31	0.66	1.40
19	-0.91	-2.21	-0.38	-0.08	1.12	0.53	1.33
20	-0.71	-	-0.41	-0.14	1.21	0.62	1.37
22	-1.19	-2.97	-0.82	-0.52	0.87	0.70	1.28
Mean	-1.01	-2.53	-0.79	-0.40	0.88	0.60	1.18
S. Dev.	0.22	0.57	0.33	0.22	0.27	0.08	0.16

these analyses are compiled in Table III. Good to excellent correlations were obtained for all except 10, for which the correlation is satisfactory. Interestingly, series 6, 7, and 14 give slightly better 100 R^2 values and significantly better F values with these single substituent constants than with any combination of dual substituent constants derived from replacement of *p*-substituted benzenes. Charton's review summarized earlier reports of σ^+ and σ^- values for these heterocycles and a comparison of these with σ^{13} values reveals expected similarities. For the electron-donating 2-furyl, 2-pyrryl, 2-thienyl, and 3-thienyl groups, the comparison is as follows (substituent, mean σ^+ value, no. of determinations, σ^{13}): 2-furyl, -0.79, 9, -1.01; 2-pyrryl, -1.66, 4, -2.53; 2-thienyl, -0.76, 12, -0.79; and 3-thienyl, -0.42, 10, -0.40. The σ^{13} values for 2-thienyl and 3-thienyl agree very well with mean σ^+ values, while those for 2-furyl and 2-pyrryl are more negative. The comparison for the electron-withdrawing pyridyl groups is as follows (substituent, mean σ^- value, no. of determinations, σ^{13}): 2-pyridyl, 0.77, 7, 0.88; 3-pyridyl, 0.63, 6, 0.60; and 4-pyridyl, 1.14, 6,1.18. Thus, the σ^{13} values for these replacement groups accord very well with mean σ^- values. In this respect, σ^{13} values for the heterocycles resemble σ^{13} values for *para*-substitured benzenes. Nonetheless, in view of the limitations of interpretation imposed by single parameter correlations, the determination of replacement substituent constants for the various dual parameter treatments is of interest.

$$\delta_X = \rho\sigma_X^{13} + C \qquad (4)$$

Dual Substituent Constants. The present data can be combined with previously reported results to establish appropriate dual substituent constants for use in eq 5-9. We have already determined α, β, and h (or f, r, and h) values from these equations for the cases in which R represents 9 *para*-substituted benzenes. All series included in the present study were utilized previously, except 14 and 22. Thus, the procedure for determining the appropriate dual

Table III. Single parameter correlations according to eq 4.

Series	r	C	100 R^2	F	n	ϵ^a
3	3.649	97.02	99.40	497.4	5	-0.68
4	5.075	82.11	97.40	149.7	6	-1.13
6	4.057	111.59	99.83	2971.1	7	-0.86
7	4.423	103.10	99.97	14737.6	7	-0.16
8	4.216	109.69	99.83	1204.7	4	-1.07
10	2.889	142.21	95.70	111.2	7	-0.99
11	4.355	133.60	97.74	216.5	7	-1.06
12	4.466	125.90	98.84	424.6	7	-0.95
14	2.717	127.61	98.98	496.1	7	-
15	4.308	95.24	99.64	829.5	5	-0.70
16	4.807	133.24	97.87	229.8	7	-1.00
17	2.818	121.59	98.99	488.3	7	-0.48
19	2.900	122.68	98.65	364.2	7	-0.58
20	3.104	119.27	98.38	243.6	6	-0.62
22	4.148	131.36	99.71	1691.0	7	-

[a] See text describing DSP-NLR correlations.

substituent constants for a given heterocycle entails performing a correlation analysis between the δ_X values for the β-vinylic carbon atom of the heterocyclic compound and the appropriate α, β, and h values for the series studied. In this

$$\delta_X = \alpha\sigma_{I,X} + \beta\sigma_{R,X} + h \qquad (5)$$

$$\delta_X = \alpha\sigma_{I,X} + \beta\sigma_{R^o,X} + h \qquad (6)$$

$$\delta_X = \alpha\sigma_{I,X} + \beta\sigma_{R(BA)} + h \qquad (7)$$

$$\delta_X = \alpha\sigma_{I,X} + \beta\sigma_{R\pm,X} + h \qquad (8)$$

$$\delta_X = fF_X + rR_X + h \qquad (9)$$

analysis, the coefficients of α and β are σ_I and σ_R (or F and R), respectively. To insure that the heterocyclic data fit the same line as that for the substituted benzenes, δ_X - h was correlated by least-squares analysis with α and β using a zero-intercept model. Accordingly, the chemical shifts for each of the 7 heterocyclic groups were used with each of the 5 equations. The replacement substituent constants of the various types thus determined are collected in Table IV. It should be noted that because σ_I appears in 4 of the equations, the σ_I values shown in these tables represent an average value for the 4 separate determinations. A single value is obtained for each of the other constants.

Table IV. Dual substituent constants for heterocycles as replacement for *para*-substituted benzenes.

	Constant						
Substituent	σ_I	σ_{R^+}	σ_{R^o}	$\sigma_{R(BA)}$	$\sigma_{R\pm}$	F	R
2-Furyl	0.54	-1.44	-0.60	-0.91	-1.46	0.99	-2.51
2-Pyrryl	-0.16	-2.30	-0.62	-1.31	-2.49	0.52	-5.09
2-Thienyl	1.81	-2.41	-1.08	-1.65	-2.32	2.49	-3.60
3-Thienyl	0.59	-0.97	-0.39	-0.55	-0.90	1.04	-1.57
2-Pyridyl	1.65	0.84	-0.45	-0.65	-0.60	2.09	-0.24
3-Pyridyl	0.35	0.10	0.04	0.13	0.24	0.57	0.63
4-Pyridyl	0.92	0.07	-0.01	0.03	0.31	1.22	1.09

To test the validity of the dual substituent constants thus obtained, the data were reanalyzed collectively with each equation. The results of these analyses are shown in Table V. This table gives the 100 R^2 value (100 times the coefficient of determination) and F value (mean square of the model divided by the mean square for the error) for each model with each series. The average 100 R^2 values for each method are as follows: $\sigma_I + \sigma_{R^+}$, 88.69; $\sigma_I + \sigma_{R^o}$, 98.77; $\sigma_I + \sigma_{R(BA)}$, 99.17; $\sigma_I + \sigma_{R\pm}$, 99.17; and F + R, 99.24. Interestingly, $\sigma_I + \sigma_{R^+}$ gave the best results for series 15; $\sigma_I + \sigma_{R^o}$ were best for series 8, 10, 14, 17, 19, and 20; $\sigma_I + \sigma_{R(BA)}$ were best for series 11, 12, and 16; and F + R were superior for series 3, 4, 6, 7, and 22. Based on the mean values cited above, however, F + R provided the best overall correlations with both types of replacement constants. Again, this accords with our previous finding that F and R gave slightly superior correlations for both *para*- and *meta*-substituted benzenes.

The use of the σ_{R^+} for electron donors and σ_{R^-} for electron-withdrawing groups, was employed initially because it seemed to give full expression to resonance effects regardless of the demand at the reaction (observation) site. Its use was prompted by an earlier finding of Krabbenhoft[14] that good correlations of the chemical shift of the β-vinylic carbon atom in β, β-dichlorostyrenes with substituent constant required the use of σ^- for the nitro group and σ^+ for other substituents. The fact that such analyses give results nearly as good as, and in some instances, better than those of other treatments suggests that there is merit in this approach. As expected, the $\sigma_{R\pm}$ values found for electron donors among the heterocycles compare very well with the σ_{R^+} values found. Accordingly, the $\sigma_{R\pm}$ values for the electron-withdrawing pyridyl groups are probably very good approximations of σ_{R^-} values.

The replacement F and R values found for the heterocycles are reasonably consistent with electronic character, as revealed by σ^{13} values. Even though they provide excellent correlations, they nonetheless probably do not represent a complete separation of field/inductive effects and resonance effects, as originally intended.[15,16] This perceived deficiency in F and R values was discussed in detail recently.[17-19] To illustrate, although the F value for 2-pyridyl is more positive, as expected, than those for 3- or 4-pyridyl, that for 4-pyridyl is more positive than that for 3-pyridyl. Since inductive and field effects should diminish with distance from the reaction site, this latter appears to be anomalous. Similarly, the large positive F value for 3-thienyl is difficult to rationalize. By the same token the sign of the R value for the 2-pyridyl group seems to be opposite of that expected. Despite these apparent inconsistencies, the F and R treatment provides the best overall 2-parameter correlations of ^{13}C data. Perhaps unfortunately, the combining of chemical intuition with scrutiny of the various constants shown in Table IV suggests that for no set has a complete separation of field/inductive and resonance effects been accomplished. Particularly, the values for 2-thienyl, 3-thienyl, and 2-pyridyl seem the most deficient in this respect.

Table V. Analyses according to eq 5-9 with heterocycles as replacements for *para*-substituted benzenes.

	Method									
	A[a]		B[b]		C[c]		D[d]		E[e]	
Series	$100R^2$	F	$100R^2$	F	$100R^2$	F	$100R^2$	F	$100R^2$	F
3	99.82	596.0	99.97	3355.2	99.96	2330.8	99.93	1442.5	99.96	2449.4
4	99.52	308.8	99.26	202.3	99.58	356.4	99.65	424.4	99.65	429.6
6	84.73	11.1	99.50	396.7	99.47	377.6	99.60	493.9	99.77	868.7
7	86.14	12.4	99.48	385.3	99.72	700.4	99.79	940.6	99.93	2933.1
8	99.07	53.0	99.98	2031.4	99.68	156.2	99.45	90.7	99.64	140.3
10	84.01	10.5	98.94	185.8	96.03	48.4	96.25	51.3	96.57	56.2
11	80.25	8.1	95.39	41.4	99.13	226.6	98.92	184.0	98.44	126.3
12	82.74	9.6	97.01	64.8	99.66	582.5	99.59	483.0	99.31	288.1
14	87.48	14.0	99.04	207.0	98.51	132.1	98.43	125.3	98.87	174.7
15	99.93	1383.8	99.75	393.2	99.61	257.1	99.83	591.6	99.80	499.2
16	83.53	10.1	95.69	44.4	99.16	236.7	99.04	206.6	98.60	140.4
17	89.26	16.6	99.72	721.4	98.91	180.7	98.96	189.8	99.43	350.4
19	87.05	13.4	99.27	270.3	98.69	150.7	98.65	146.2	99.13	227.3
20	82.75	7.2	99.77	652.4	99.72	538.1	99.69	478.3	99.72	533.3
22	84.05	10.5	98.77	160.2	99.77	871.0	99.82	1082.9	99.82	1088.1

[a] $\sigma_I + \sigma_{R^+}$. [b] $\sigma_I + \sigma_{R^0}$. [c] $\sigma_I + \sigma_{R(BA)}$. [d] $\sigma_I + \sigma_{R\pm}$. [e] F + R.

The present findings reinforce a notion that has evolved concerning the DSP approach. That different σ_R scales give better results with several of these seemingly very closely related structural series is in accord with the interpretation that a nonlinear electronic demand operates from the measurement site (in this case, at the β-carbon atom of the vinylic side-chain) and that substituent response depends upon structural demand by the side chain. To accommodate similar circumstances, Bromilow, Brownlee, Craik, Sadek, and Taft have suggested a NSP-NLR relationship, shown in10, that

$$\delta_X = \rho_I\sigma_I + \rho_R\sigma_R{}^o/(1-\epsilon\sigma_R{}^o) \qquad (10)$$

allows for such non-linearity of resonance demands.[20] In this equation, the resonance term is modified by the inclusion of a parameter, ε, that scales the $\sigma_R{}^o$ term. Accordingly, it was felt that a single σ_R scale could not be devised to cover all electronic circumstances and that a given substituent might require an infinite number of σ_R values, each depending upon the situation in question. Unfortunately, at present there is normally no way to judge *a priori* what ε should be for a given reaction series. Consequently, the authors suggested that correlations be based on multiple calculations that start with $\epsilon=0$ and arrive at the best possible value by successive incrementation. It was also found that the treatment fails when ε lies outside the limits of ±1.5. While this treatment continues to represent, technically, a DSP approach, the difficulty in predicting an appropriate ε value for a given analysis will sometimes introduce an essentially disposable parameter that detracts from the method.

Nonetheless, it was of interest to apply the DSP-NLR method to the present data to see if improvements in the $\sigma_R{}^o$ correlations could be obtained. Such a treatment is enabled in the present case because the ε for the various vinylic side-chains can be calculated using the suggested procedure and the previously obtained ^{13}C absorption data for *p*-substituted styrenes.[11] These values, calculated to the nearest 0.01, are included in Table II. Interestingly, application of the DSP-NLR method to the heterocyclic data using the ε values obtained in this manner permits the separate analysis of all data for each heterocycle. This could not be done using other DSP approaches because of the constancy of σ_I and σ_R values (or F and R) for each heterocycle throughout all series. The DSP-NLR results are collected in Table VI. The 2-furyl data give an excellent correlation and those for 2-pyrryl, 3-pyridyl, and 4-pyridyl give good correlations. Perhaps not surprisingly in light of the foregoing, 2-thienyl, 3-thienyl, and 2-pyridyl give distinctly poorer results. This approach could lead to erroneous results through several possible sources of error which cannot atpresent be distinguished. The previous suspicion that $\sigma_R{}^o$ for the latter three heterocycles may not reflect a complete separation of resonance effects is one possible source. Unappreciated ring anisotropies or other geometrical effects could be significant. Finally, it may not be appropriate to utilize the same ε values for the side chains when they

Table VI. DSP-NLR results using eq 10.[a]

Substituent	100 x R^2	F
2-Furyl	99.11	610.8
2-Pyrryl	97.00	129.6
2-Thienyl	82.73	26.3
3-Thienyl	94.48	102.7
2-Pyridyl	96.02	84.5
3-Pyridyl	97.37	184.8
4-Pyridyl	97.02	162.9

[a] δ_X-h was allowed to regress on $\sigma_I + \sigma_R{}^o/(1-\epsilon\sigma_R{}^o)$. The values of h were obtained from the intercepts of the regressions of δ_X on $\sigma_I + \sigma_R$ for *para*-substitured styrenes. ε values were obtained as described in the text.

are attached to heterocycles as when they are attached to substituted benzenes. If this latter is true, however, the DSP-NLR treatment would be severely limited, since this situation would carry the implication of non-constancy of ε values.

As an alternate view of the problems arising from the use of multiple σ_R scales in the DSP treatment, Aganas'ev has proposed that the deficiencies are simply rooted in errors in the substituent constants.[21-24] However, a reanalysis of the *para*-substituted benzene data from the previous report[11] using his σ^* and σ_r gave correlations distinctly inferior to those of DSP treatments using Taft scales[4] or the Swain-Lupton treatment using the updated F and R values.[15] Again, this reinforces the view that no single set of DSP constants can be devised that will be universally applicable.

Godfrey[25,26] has recently offered an interpretation of why the dual parameter analysis of substitutent effects fails, but the application of his interpretation to replacement substituent constants is not obvious.

Conclusions

The ^{13}C nmr method for defining substituent constants is applicable to replacement constants for heterocyclic rings. For the 7 heterocyclic replacements considered in this report, the best set of single substituent constants is one in which constants for electron-donating groups resemble σ^+ values and those for electron-withdrawing groups resemble σ^- values. Values for σ_I and the various σ_R scales for the Taft DSP treatments can also be established by the ^{13}C method. σ_I and $\sigma_R o$ values found by the present method do not, in the main, agree with similar values previously reported from the analysis of infrared adsorptions. Swain-Lupton constants, F and R, provide slightly superior nmr correlations compared to those of any single DSP treatment. The DSP-NLR method can be applied to the present results because ε values have been determined for the side-chains from corresponding substituted styrenes. The results are possibly indicative that a separation of field/inductive effects from resonance effects has not been achieved for 2-thienyl, 3-thienyl, and 2-pyridyl. The other four heterocyclic attachments are unexceptional. Afanas'ev constants, σ^* and σ_r, do not improve correlations of ^{13}C nmr data over those of appropriate Taft constants in DSP treatments. Despite apparent internal inconsistencies in the values of F and R constants, the Swain-Lupton treatment of heterocyclic replacement constants seems to be the best overall method for correlating ^{13}C data.

References

1. Based on work presented by Leonard J. Wiseman, Jr., in partial fulfillment of the requirements for the M.S. degree, Memphis State University, May, 1983.
2. Jaffe, H. H. *Chem Rev.* 1953, *53*, 191-261.
3. Charton, M. In "Correlation Analysis in Chemistry"; Chapman, N. B.; Shorter, J. Eds.; Plenum Press: New York, 1978, Chapter 5.
4. Ehrenson, S.; Brownlee, R. T. C.; Taft, R. W. *Prog. Phys. Org. Chem.* 1973, *10*, 1-80 gives a thorough review of this treatment.
5. Yukawa, Y.; Tsuno, Y. *Bull. Chem Soc. Jpn.* 1959, *32*, 971-981.
6. Charton, M. *Prog. Phys. Org. Chem.* 1981, *13*, 119-251.
7. Tupitsyn, I. F.; Zatsepina, N. N.; Kolodina, N. S.; Kaminskii, Yu. L. *Reakts. Spos. Org. Soedinenii* 1969, *6*, 458-467.
8. Kaminiskii, Yu, L. *Reakts. Spos. Org. Soedinenii* 1969, *6*, 797-809.
9. Angelelli, J. M.; Katritzky, A. R.; Pinzelli, R. F.; Topsom, R. D. *Tetrahedron* 1972, *28*, 2037-2050.
10. Robinson, C. N.; Slater, C. D.; Covington, J. S.; Chang, C. R.; Dewey, L. S.; Franceschini, J. M.; Norris, D. W.; Rodman, L.; Smith, V. I.; Stablein, G. E.; Fritzsche, J. L.; Hamilton, L.; Irving, C. C. Jr.; Morris, J. M.; Ward, F. E. *J. Magn. Res.* 1980, *41*, 293-301.

11. Slater, C. D.; Robinson, C. N.; Bies, R.; Bryan, D. W.; Chang, K.; Hill, A. W.; Moore, W. H. Jr.; Otey, T. G.; Poppelreiter, M. L.; Reisser, J. R.; Stablein, G. E.; Waddy, V. P. III; Wilkinson, W. O.; Wray, W. A. *J. Org. Chem.* 1985, *50*, 4125-4130.

12. Jones, G. In "Organic Reactions," Vol. 15, Adams, R.; Blatt, A. H.; Boekelheide, V.; Cairns, T. L.; Cope, A. C.; Cram, D. J.; House, H. O., Eds.; John Wiley and Sons: New York, 1967, Chapter 2.

13. All statistical calculations were done by use of the SAS program available from the SAS Institute, Inc., Box 8000, Cary, NC 27511.

14. Krabbenhoft, H. O. *J. Org. Chem.* 1978, *43*, 1830-1832.

15. Swain, C. G.; Lupton, E. C., Jr. *J. Am. Chem. Soc.* 1968, *90*, 4328-4337.

16. Swain, C. G.; Unger, S. H.; Rosenquist, N. R.; Swain, M. S. *J. Am. Chem. Soc.* 1983, *105*, 492-502.

17. Reynolds, W. F.; Topsom, R. D. *J. Org. Chem.* 1984, *49*, 1989-1992.

18. Hoefnagel, A. J.; Oosterbeek, W.; Wepster, B. M. *J. Org. Chem.* 1984, *49*, 1993-1997.

19. Charton, M. *J. Org. Chem.* 1984, *49*, 1997-2001.

20. Bromilow, J.; Brownlee, R. T. C.; Craik, D. J.; Sadek, M.; Taft, R. W. *J. Org. Chem* 1980, *45*, 2429-2438.

21. Afanas'ev, I. B. *Int. J. Chem Kinetics* 1981, *XIII*, 173-816.

22. Afanas'ev, I. B. *J. Org.Chem. U.S.S.R.* 1981, *17*, 373-386.

23. Afanas'ev, I. B. Trojanker, V. L. *Org. Magn. Res.* 1982, *18*, 22-27.

24. Afanas'ev, I. B. *J. Gen.Chem. U.S.S.R.* 1984, *54*, 746-753.

25. Fadhil, G. F.; Godfrey, M. *J. Chem. Soc., Perkin Trans. 2* 1988, 133-137.

26. Godfrey, M. *J. Chem. Soc., Perkin Trans. 2* 1988, 139-142.